Interventions to Reduce Aerosolized Microbes in Dental Practice: A Systematic Review with Network Meta-analysis of Randomized Controlled Trials

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Abstract: The aim of this systematic review and network meta-analysis was to identify and rank the effectiveness of different interventions used in dental practice to reduce microbial load in aerosolized compounds. Seven electronic databases were searched to April 6, 2020, for randomized controlled trials (RCTs) or nonrandomized prospective studies in the field. Study selection, data extraction, and risk-of-bias assessment were performed for all included studies, while the outcome of interest pertained to differences in bacterial load quantification through the use of different interventions prior to aerosol-generating procedures in dental practices. Random effects frequentist network meta-analysis was performed, with mean difference (MD) and 95% CI as the effect measure. Confidence in the documented evidence was assessed through the newly fueled CINeMA framework (Confidence in Network Meta-analysis) based on the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation). Twenty-nine clinical trials were deemed eligible, 21 RCTs and 8 nonrandomized studies, while 11 RCTs contributed to the network meta-analysis, comprising 10 competing interventions. Tempered chlorhexidine (CHX) 0.2% as compared with nonactive control mouth rinse, prior to routine ultrasonic scaling, was most effective toward reduced postprocedural bacterial load with an MD of −0.92 (95% CI, −1.54 to −0.29) in log<jats:sub>10</jats:sub> bacterial CFUs (colony-forming units). For CHX 0.2%, an MD of −0.74 (95% CI, −1.07 to −0.40) was observed as compared with control. Tempered CHX 0.2% presented the highest probabilities of being ranked the most effective treatment (31.2%). Level of confidence varied from very low to moderate across all formulated comparisons. These findings summarize the current state of research evidence in the field of aerosolized bacteria in dentistry. Instigated by the era of SARS-CoV-2 pandemic, the stipulation of a broader evaluation of the aerosolized microbes, including viruses, potentially coupled with disinfectant-based prevention schemes should be prioritized.

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Interventions to reduce aerosolized microbes in dental practice. A Systematic Review with Network Meta-analysis of Randomized Controlled Trials

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Abstract

The aim of this systematic review and network meta-analysis was to identify and rank the effectiveness of different interventions used in dental practice to reduce microbial load from aerosolized compounds. Seven electronic databases were searched to April 6, 2020 for randomised controlled trials (RCTs) or controlled clinical trials (nRS) in the field. Study selection, data extraction and risk of bias assessment was performed for all included studies, while the outcome of interest pertained to difference in bacterial load quantification through the use of different interventions prior to aerosol-generating procedures in dental practices. Random effects frequentist network meta-analysis (NMA) was performed, using mean difference (MD) and 95% confidence intervals (95% CIs) as the effect measure. Confidence in the documented evidence was assessed through the newly fueled CINeMA framework based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Twenty nine clinical trials were deemed eligible, with 21 RCTs and 8 nRS, while 11 RCTs contributed to the network meta-analysis, comprising of 10 competing interventions. Tempered chlorhexidine (CHX) 0.2% compared to non- active control mouthrinse, prior to routine ultrasonic scaling, was most effective towards reduced post- procedural bacterial load with a MD -0.92 (95% CI: -1.54, -0.29) in $\log_{10}$ (colony forming units) CFUs of bacteria. For CHX 0.2% a MD of -0.74 with 95 CI%: -1.07, -0.40 was observed, compared to control. Tempered CHX 0.2% presented the highest probabilities of being ranked as the most effective treatment (31.2%). Level of confidence varied from very low to moderate across all formulated comparisons. Findings reflect the current state of evidence framed by research in the field of aerosolized bacteria. In the era of SARS-CoV-2 pandemic, the stipulation of a broader evaluation of the aerosolized microbes, including viruses, potentially coupled with disinfectant treatment schemes should be prioritized.

Keywords: aerosol, spatter, droplet, bacteria, microbial load, SARS-CoV-2, COVID-19, dentistry, ultrasonic scaling, debonding, mouthrinse

Introduction

Working environment of dentists of practically all clinical subjects rests them exposed, almost universally and in everyday practice to certain potential hazards, related on one part to airborne material particulates produced during and/ or after practicing on composites/ restorations, with high rotary instrumentation (Ireland et al. 2003; Cokic et al. 2020), but also allied to potentially infectious bacteria, viruses or other microorganisms residing in the patients' oral cavity (Dawson et al. 2016). Aerosolized microorganisms, including potentially airborne pathogens may come as a result of active performance of high-powered handpiece utilization during standard dental procedures. Tooth grinding for restorations, material grinding, composite removal after orthodontic debonding, attachment grinding after aligner treatment (Iliadi et al. 2020), or routine practice professional oral prophylaxis using high-speed ultrasonic scalers, are adequately matched for an increased dynamic for spatter related contamination, within the dental practice environment and across the practices' personnel (Laheij et al. 2012).

In particular, the potentially pathogenic capacity of aerosols produced in dentistry depends on the combination of in-service compressed air and water spray with tooth and material debris, plaque, blood, calculus and saliva mixture, especially allied to patient's dynamic for an airborne disease. On top of that, increasing research interest has long identified the role of microorganisms being present within the dental unit waterlines' (DUWL) and as such, their potential to mix- up with oral cavity patient-hosting risk factors, namely blood and saliva. Following the above, aerosols may set a risk for disease transmission and cross contamination within the dental clinic environment, however, this in turn is largely dependent on patients' pathogenic potential and positivity for induction of an airborne disease (Harrel and Molinari 2004; Laheij et al. 2012).

An array of interventions have been proposed over a considerable amount of time to reduce environmental and/or patient/professional related aerosol induced contamination, mainly directed towards the use of antiseptic agents as pre- procedural mouthwash rinse solutions (Logothetis and Martinez-Welles 1995; Sethi et al. 2019). Use of alternative schemes have also been reported, such as high volume evacuators (Holloman et al. 2015), or in-service instrumentation coolant agents (Jawade et al. 2016) and antiseptic agents directly applied to the DUWLs (Mamajiwala et al. 2018).

Since more than 20 years, the American Dental Association (ADA) council on scientific affairs and dental practice, has included recommendations for infection control against spatter and droplet forming aerosols. Protective eyewear, high volume evacuator, appropriate positioning of the patients and rubber dams were recognized as the foremost protection strategies (ADA Council 1996). Latest reports appear to focus on specific occupational practices, identified as most prone to bio-aerosol stimulation, with those being the performance of oral prophylaxis measures in- office, through ultrasonic scaling (Joshi et al. 2017; Sethi et al. 2019), but also enamel clean- up practices after orthodontic fixed appliance debonding with high speed instrumentation (Dawson et al. 2016).

Currently, there is no high- quality evidence stemming from a systematic review or meta-analysis about in- office protective measures, when aerosol generating procedures are upheld, with regard to microbial air contamination. This includes a variety of patient profiles proceeding to the dental office, including all ages or periodontal conditions, and targets on identifying the most effective range of interventions. It seems timely, that an evaluation and ranking of the existing evidence with regard to measures taken to reduce microbial dissemination through aerosols in dental practice is endorsed. Therefore, our aim was to collectively and systematically appraise current literature and evidence on interventions upheld to minimize aerosol contamination in dental office and provide a conceivable ranking of the effectiveness of the existing approaches.

Materials and Methods

Protocol, Registration and Reporting

The protocol of this study was registered with the Open Science Framework (https://osf.io/ewph9/) (Koletsi et al. 2020). Reporting was conducted in line with the PRISMA guidelines extension for network meta-analysis (Hutton et al. 2015). The decision to undertake a network meta-analysis was based on the availability of included studies and variety/ multitude of interventions, the multi- arm design of the included studies and the focus on a similar outcome. As such, all available evidence including direct and indirect comparisons of interventions were considered, thus offering an increased amount of data being synthesized to achieve a pooled and more precise estimate.

Eligibility criteria

Eligibility criteria for study selection were determined as follows:

- Study design: randomized controlled trials or prospective clinical trials comparing at least 2 interventions

- Participants: patients proceeding to dental office/ university/ hospital settings for typical dental procedures such as, but not confined to: ultrasonic scaling, enamel clean- up procedures during orthodontic bracket debonding after fixed appliance treatment, restorative procedures

- Intervention: any type of active intervention to reduce aerosol contamination in dental practice

- Comparator: alternative active intervention strategies, or control interventions (ie, no intervention, water, normal saline)

- Outcome: any outcome related to microbial count measurement in droplets/ aerosol after dental procedures. Logarithmic transformation was used to maintain a consistent effect measure across studies included in the quantitative synthesis

- Exclusion criteria: pilot studies with 5 or less participants per group, retrospective study designs.

Search strategy and study selection

Electronic searching was conducted within both published and unpublished research, across 7 databases, with no restriction (Appendix Table 1). Medline via Pubmed, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR) we searched. Moreover, unpublished literature was searched in the Open Grey, the ClinicalTrials.gov (www.clinicaltrials.gov), the National Research Register (www.controlled-trials.com). Hand searching of the eligible for inclusion articles was employed for any additional potential inclusion and authors of the included papers were contacted when needed to clarify on data extraction or data curation. The date of search was April 6, 2020. Keywords involved, but were not restricted to “aerosol”, “spatter”, “droplet”, “ultrasonic”, “composite removal” and “bacterial count”, “microbial load”.

Technical description details of the methodology regarding: data collection, risk of bias assessment, summary measures and data syntheses, assessment of the quality of the evidence and assessment of

confidence in the estimated effect, publication bias, additional analyses are available in the *Appendix* file (Appendix text).

Stata version 15.1 software was used for all analyses (StataCorp, College Station, Texas, USA).

Results

Search Strategy and Details

The initial search yielded 266 articles from electronic databases and hand- searching. After title and abstract screening, the number of remaining articles for full text evaluation was 35. Of these, 29 were eligible for qualitative synthesis (Appendix Reference 1, presents references of all included studies), while 11 were eventually included in a network of studies contributing to meta-analyses (Feres et al. 2010; Reddy et al. 2012; Gupta et al. 2014; Kaur et al. 2014; Rani et al. 2014; Holloman et al. 2015; Saini 2015; Mohan and Jagannathan 2016; Joshi et al. 2017; Retamal-Valdes et al. 2017; Waghmare et al. 2018) (Figure 1).

Study design and characteristics

An overall picture of information on the included studies is outlined in Table 1. Of the 29 studies, the majority were RCTs (21/ 29; 72.4%), with the rest being non- randomised clinical trials. Publication period spread across almost 30 years, ranging from 1992 to 2020. A considerable amount of studies was published within the last decade (24/ 29; 82.8%), with 15 out of 24, since 2015. Parallel trials predominated (23/ 29; 79.3%), while the number of patients contributing each studies' findings ranged from 18 to 120 across the study samples.

Further detailed description of the results of study characteristics related to interventions, and outcome assessment, risk of bias assessment, single- study findings and additional analyses are presented in the *Appendix* file (Appendix text).

Effects of Interventions and Network Meta-analysis

After consideration of clinical heterogeneity and consistency parameters, such as study design, similarity of outcomes, populations and procedural interventions, 13 RCTs were eligible for inclusion in the network meta-analysis, while 11 studies ultimately contributed to network generation. In two studies (Shetty et al. 2013; Swaminathan et al. 2014), no data or distributional parameters of the samples were readily available or could be inferred from the published article within text, figures or tables, whilst communication with authors was attempted but still remained unsuccessful. Of the 21 RCTs in total, eight were non- eligible and the reasons were related to non- comparable procedural settings, that is, interventions for air- polishing (Logothetis and Martinez-Welles 1995), as ultrasonic liquid coolers (Jawade et al. 2016; Sethi et al. 2019), as added solutions in DUWL (Mamajiwala et al. 2018), due to correlated study design (Fine et al. 1992; King et al. 1997), or non- comparable assessment of the outcome and use of effect measure. Non- randomized studies were a priori excluded from the network meta-analysis, following the design of the protocol.

The network map of the included interventions and their contribution and comparisons within the network is presented in Figure 2, while all interventions were examined under a setting of procedural ultrasonic scaler in- practice, in adult patients. A total of 16 direct and 29 indirect comparisons were ultimately formulated across contributing studies and competing interventions. The contribution plot of the impact of each direct comparison using percentage weight squares is shown in Appendix Figure 1. For example, for the comparison between high volume evacuator (HVE) and control, there is no indirect evidence and 100% of the information comes from the direct evidence. A set of single study effects and pooled estimates of the respective direct pairwise comparisons is presented in Appendix Figure 2. The results of the network meta-analysis, following an augmented format under multivariate meta-analysis (Ian White 2015), are collectively presented in Table 2 and also in Appendix Figure 3. As noted, tempered chlorhexidine (CHX) 0.2% compared to control was most effective towards reduced post- procedural bacterial load with a mean difference (MD) of -0.92 (95% CI: -1.54, -0.29) in $\log_{10}$ CFUs. A similar trend was noted for CHX 0.2% compared to control (MD: -0.74; 95 CI%: -1.07, -0.40), as well as for chloride dioxide (ClO_2) versus control (MD: -0.68; 95%CI: -1.01, -0.34).

Test for inconsistency across the network of direct and indirect comparisons, beyond what could have been explained by chance alone, was not significant (p=0.99). Inconsistency plot, assuming loop-

specific heterogeneity estimates did not reveal evidence of inconsistency (Appendix Figure 4). Inconsistency was also not detected after fitting the node- splitting model (White 2015). The presence and effect of two potential effect modifiers was also inspected, to allow for any potential detection of violation of the assumption of transitivity. These modifiers were pre- determined to population related (ie, chronic periodontitis sample groups), as well as types of pathogen analysis cultures (ie, aerobic/ anaerobic). No evidence of uneven distribution across different comparisons of interventions was detected (test for inconsistency, p=0.98).

Ranking of the interventions of the network in order of effectiveness, towards induction of reduced microbial load, from aerosols produced during ultrasonic in- practice service revealed the following, based on both the cumulative probability of intervention effectiveness, as well as the probability of being ranked as best treatment of choice: the tempered CHX 0.2% at 47^{o}C was ranked as the most effective in achieving reduced bacterial load after the use of ultrasonic scaling in dental practice both with regard to overall % SUCRA value (78.6%), as well as with respect to being the most likely intervention to be ranked as 1st treatment of choice (31.2%) (Figure 3; Appendix Table 4). In terms of overall SUCRA values for effectiveness, the tempered CHX 0.2% was followed by conventional CHX 0.2% (66.4%), ClO_2, (59.0%) and ozone (OZ) (57.2%) (Appendix Table 4; Appendix Figure 5). In terms of being the "1st treatment of choice", it was followed by OZ (19.2%), CHX 0.12% (16.9) and povidone iodine (PI) (11.3%).

Quality of the evidence and confidence in the estimated effect

The assessment of the quality of the evidence for the comparisons of the identified 4 most effective interventions according to SUCRA values of ranking, including the non- active control intervention, revealed a range of very low to moderate level of confidence for the results of the current network meta-analysis based on the CINeMA framework originally framed on GRADE, overall and across comparisons. The most prevalent reason for downgrading confidence levels was within study bias, thus raising "some concerns", with all contributing comparisons being prone to this limitation. Likewise, imprecision was also an issue, mostly from indirect evidence. Major concerns were raised with regard to imprecision, solely in comparisons related to OZ. Moderate confidence levels were framed for

comparisons related to tempered CHX 0.2%, conventional CHX 0.2% and ClO_2, all compared to control (Figure 4).

Discussion

Findings in context

Major concerns have been raised with regard to working environment of health care professionals and major efforts are endorsed to minimize the dissemination of microbial and potentially pathogenic load of generated aerosols across medical disciplines, which has been particularly vital in the era of a pandemic (Coronavirus situation report 2020). Dental practice is one of the frontline representatives of high risk population against aerosolized particulates, including bacterial, viral and fungal pathogens (Laheij et al. 2012). Workforce involved are constantly confronted with potentially hazardous compounds as a by- product of standard care delivery to patients; this, might be particularly alarming since small- sized particulates have long been considered as respiratory system triggering proxies, even making their way deeply within the lungs (Oberdörster et al. 2005; Napierska et al. 2010; Dawson et al. 2016). Aforementioned concerns are augmented by latest awareness of microbial spread, air suspension and stability in aerosols and on surfaces. An up- to date report, based on experimentally induced simulations, has suggested that stability kinetics of severe acute respiratory- syndrome-related coronaviruses (both SARS-CoV-1 and SARS-CoV-2) may rest them viable in aerosols for at least 3 hours, albeit in reduced infectious titer (van Doremalen et al. 2020). The presence and detectability of SARS-CoV-2 in saliva of infected patients imposes an additional risk for its air- suspension after an aerosol- generating dental procedure (Azzi et al. 2020). To this line, identification of interventions with a refined dynamic of reduction of the microbial load detected after aerosol generating procedures in dental practice environment in general, is considered an important contribution to clinical evidence base. Implications for decision making and safety considerations within high risk occupational environments for patients and healthcare professionals alike are indisputably on the way, their enforcement being particularly necessitated by the existence of seasonal pandemics.

The findings of the present systematic review are framed based on the eligibility and reporting competence of the existing evidence base with regard to aerosol microbial contamination in dentistry. A sound emphasis on interventional designs with an a priori potential of providing minimally biased

estimates for efficacy of competing treatments was sought. As such, the most prevalent dental procedure under the microscope of this review pertained to ultrasonic scaling, bearing an explicit dynamic of generating aerosolized microbes. Pre- procedural mouth rinse with tempered CHX 0.2% at 47^{o}C prevailed as the treatment with the highest probabilities of being opted as the most effective intervention in terms of reducing bacterial counts after ultrasonic scaling in practice, when measured through air sampling within a distance of 90 cm from the dental unit. Other documented intervention alternatives bearing high probabilities of being selected as effective first line treatment alternatives or overall were OZ, standard CHX 0.2% or 0.12%, PI and ClO_2.

Use of chlorhexidine in dentistry has been well-reported mainly as a large-scale disinfectant towards the management of gingival inflammation and plaque control (Al-Maweri et al. 2020), but also as an adjunct to mechanical therapy in chronic periodontitis patients (Herrera et al. 2020). The most recent report from the Cochrane collaboration has identified the use of CHX mouth rinse, irrespective of concentration and as an adjunct to standard mechanical hygiene measures, as particularly effective in terms of dental plaque reduction and management of mild gingivitis. These claims have been supported by high quality evidence (James et al. 2017). However, adverse effects have also been in place, namely, taste disturbance, mucosal ulceration, burning sensation or oral mucosa soreness. To this respect, alternate CHX kinetics have been described early on by Konig et al, 2002, when testing the use of tempered CHX 0.2% at 47^{o}C as a mouthrinse for plaque control. Temperature selection was based on safety considerations for preventing any pulpal or mucosal adverse effect, while the tempered solution revealed an increased efficacy against microbial plaque accumulation. Irrigation with tempered CHX solution also demonstrated an increased potential for bacterial counts elimination (König et al. 2002). These early findings on within oral cavity disinfection agents, are in agreement with the results of the present review, as well as with original clinical reports on reducing aerosol contamination after ultrasonic scaler use (Reddy et al. 2012; Joshi et al. 2017). Notwithstanding this, practical implications may come into light when considering routine use of tempered anti- microbial solutions in dental office. Standard temperature CHX solution should be heated in a thermostatically regulated water bath individually prior to clinical use in order to produce CHX at 47^{o}C, thus rendering the procedure additionally complicated, as far as practice management is concerned.

Periodontal research and identification of interventions that could reduce the plaque microbial/ bacterial load or act as therapeutic adjuncts to gingival inflammation, has been the backbone of research in aerosolized microbes in dentistry. Povidone Iodine (PI), ozone (OZ) or chlorine dioxide (ClO_2) have been identified by the present NMA as potentially effective agents against bacterial aerosol contamination, while alternative applications of these agents constitute disinfection practices in the treatment of periodontitis (Yadav et al. 2015; Perrella et al. 2016; Gandhi et al. 2019). Alternative effects and actions of PI, OZ, and ClO_2 related to certain pathogen types due to their oxidation potential in reaction with virus cell structure, is also provided in the *Appendix* file (Appendix text).

As most published research on dental aerosols comes from reports on bacterial counts, a fragment of those have examined implication specific species. An array of 38 types of pathogens have been recognized in the latest scoping review in the field (Zemouri et al. 2017). It was interesting that identified micro- organisms included 16 bacterial species and 23 fungal species, while none pertained to parasites or viruses. However, this reflects the simultaneous abundance and scarcity of research paths across different directions. To the boundaries of the present systematic review, the bulk of included studies focused on a universal identification and assessment of the bacterial load as a whole, with no further perspectives on underlying species. Checkerboard DNA-DNA hybridization technique was implemented sporadically and solely in two studies (Feres et al. 2010; Retamal-Valdes et al. 2017) to identify microbial composition. A close observation of the microbial complexes, revealed an increased prevalence of species of the “orange complex” in aerosols produced after ultrasonic scaler use, which are mostly represented by the *Fusobacterium* family. The presence of fusobacterium was higher in absence of any active pre- procedural mouthrinse intervention. *Fusobacterium nucleatum* has been implicated in the initiation and progression of periodontitis, while its role has been identified as inhibitory of gingival fibroblast or gingiva- derived mesenchymal cell proliferation, intracellular reactive oxygen species generation, and promotive of cellular apoptosis (Kang et al. 2019); furthermore, *Fusobacterium nucleatum* infection has been linked to other pathologic ophthalmic and respiratory conditions (Bhattacharya et al. 2005). Yet, studies using checkerboard DNA-DNA hybridization are close-ended and can only reveal the absence, presence and levels of the targeted bacterial species, in this instance periodontal pathogens. This does not exclude the possibility that many other species not

included in the pre-selected DNA-probe panel will also be present in the aerosol, but not able to be identified.

The role of DUWLs in the formation of contagious spatter compounds is regarded pivotal and as being the counterpart to patient- related aerosol mixes. Although, under the scope of the present review, only one study (Mamajiwala et al. 2018) pertaining to the assessment of effectiveness of different measures of DUWL disinfection, on airborne sampling could be identified, the use of specific add-ins such as CHX as solution extracts, has been proven beneficial in reducing both aerobic and anaerobic bacterial counts originating from aerosols. Furthermore and albeit the fact that the vast majority of research has evaluated microbiota of the waterlines per se, with no speculation about subsequent aerosol formation and its implications, there is increasing awareness regarding the potential health risk problems arising from a contaminated water- supply entry and colonization of pathogenic microbial species. *Mycobacteria, helicobacter pylori, Legionella pneumophilla* as well as *Pseudomonas spp* are some of the implicated species (Giacomuzzi et al. 2019; Castellano Realpe et al. 2020; Tuvo et al. 2020). Water filters installation, shock disinfection of hydrogen peroxide with concentrations ranging from 3% to 6% v/v, chlorhexidine, or specially designed biofilm removing systems have been proposed (Baudet et al. 2020).

In all, adoption of occupational measures in dental practice against potentially hazardous aerosol forming procedures should be considered in a universal basis and standard precaution procedures should involve more skeptical application and even reduction in the use of aerosol forming instrumentation in everyday practice. These constitute not only ultrasonic scaling, but also restorative procedures (Purohit et al. 2009), enamel clean- up after fixed appliance orthodontic treatment (Dawson et al. 2016) or massive attachment removal following aligner treatment (Iliadi et al. 2020)(Iliadi 2020). To this respect, founding recommendations from the U.S. Centers for Disease Control and Prevention (CDC Report 2016) involve a range of safety considerations, as documented by aerosol and waterline precautions, personal protective equipment and ventilation management.

Strengths and Limitations

This is the first large scale systematic review with network meta-analysis in intervention practices to reduce pathogen load of aerosols within dental practice environment. The design of this review allows

for certain advantages to be considered. First, the study involved a priori registration to an open access registry, as well as a reporting framework based on contemporary available guidelines specific for the design of the network meta-analysis, safeguarding against reporting bias. Second, a number of electronic databases within published and unpublished literature, with no restrictions was searched, thus eliminating the potential for publication bias. Third, a rigorous approach was followed, involving a network set- up of the existing intervention strategies. Network meta-analysis in general allow for indirect comparisons between pairwise interventions not directly tested across original studies, thus providing additional and potentially more precise information for the estimated effect across treatments (Caldwell et al. 2015). Fourth, the simultaneous assessment of all available interventions allows for an estimation of their relative ranking for a specific outcome, which is non- applicable for conventional meta-analyses (Chaimani et al. 2019).

Limitations do exist as well, while they are consistently inherent to the contributing primary studies included in the review. Apart from identified issues with the internal validity over an amount of included studies, aerosolized products were solely considered in terms of bacterial load and their pathogenicity could not be measured. The vast majority of interventions were also checked under the settings of ultrasonic scaling in practice; however, extrapolation to other spray, or- high speed handpiece comprising settings may not be considered unfeasible or unrealistic.

Conclusion and Implications for Research

Allowing for all discussed caveats, the findings of the present network meta-analysis suggest the use of pre- procedural mouthrinse with preferably tempered chlorhexidine as the most effective strategy for the reduction of aerosol related bacterial load in dental practice. In addition, in temporal conditions dictated by seasonal epidemics of other forms of pathogens, mostly represented by oxidative stress-vulnerable viruses, substitute intervention strategies, such as povidone iodine might be considered as viable solutions. In this respect, research towards identification of additionally tested disinfectant agents used as mouthwash rinses should also be endorsed. However, for all latter approaches, a clear stipulation for robustly conducted and reported clinical trials is indisputable.

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Author contributions: TE conceived the idea for this study, assisted in data collection, risk of bias assessment; DK, organized the study set- up, did the data extraction, risk of bias assessment, statistical data analysis and wrote the first draft of the manuscript; DK, GNB and TE contributed to study design and critically revised the manuscript; All authors gave their final approval and agree to be accountable for all aspects of the work.

FIGURE LEGENDS

Figure 1. Flow chart of study selection.

Figure 2. Network plot, with all contributing interventions and their comparison matrix. Edge colors indicate risk of bias (RoB) of the contributing studies to the relative comparisons (green: “low RoB”; yellow: “some concerns”). Size of the blue nodes is analogous to the contribution of the sample size for each intervention overall.

Figure 3. Rankograms for the 10 competing interventions. Horizontal axis describes the order of the ranks, while vertical shows the probability (0- 1 scale) of each intervention to be ranked 1^{st}, 2^{nd}, …10^{th}, in terms of effectiveness for decreased pathogen load after ultrasonic scaler usage.

Figure 4. CINeMA framework confidence table representing evidence ratings between the four interventions with the highest SUCRA value, as well as the non- active control treatment.

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Table1. Characteristics of the included studies (n=29), in alphabetical order.

Study ID	Participants	Intervention (one or >1)	Comparator (one or >1)	Outcome
Dawson et al, 2016 nRS, parallel- 3 arm Setting: hospital orthodontic department	18 patients at *orthodontic bracket debonding*; age NR; air sampling for 15 minutes during debonding (including chairside high volume aspirator)	1. slow-speed handpiece, 0.2% CHX gluconate PMR 2. slow-speed handpiece, sterile water PMR Rinse duration: 1 minute	Slow-speed handpiece, no PMR	Bacterial load in CFUs (anaerobic culture), with PCR and DGGE, at 30 cm sampling distance [no mouthrinse performed better]
Devker et al, 2012 nRS, parallel- 3 arm (plus within group control) Setting: NR	90 patients; age 18- 45; air sampling for 10 minutes during ultrasonic scaling Split- mouth controls used in each group	1. 0.2% CHX prior to scaling Rinse duration: 2 minutes 2. HVE attachment used during ultrasonic scaling (140 mm Hg)	Combination of 0.2% CHX plus HVE attachment Rinse duration: 2 minutes	Bacterial load in CFUs (aerobic culture), with blood agar plates and colony counters, at 15, 30, 90 cm sampling distance
dos Santos et al, 2014 nRS, cross- over Setting: university	23 patients during *orthodontic treatment* (at dental prophylaxis procedure with aerosolized sodium bicarbonate); age: 10-40; air sampling for 4 minutes during prophylaxis procedure	0.2% CHX PMR Rinse duration:1 minute	No PMR	Bacterial load (aerobic culture) in CFUs, with blood agar plates and colony counters, at no measurable sampling distance (reports: clinician's face, 10cm lower than the mouth, patient's thoracic region)
Feres et al, 2010 RCT, parallel 4- arm Setting: university	60 patients (not advanced periodontitis); age 30- 70; air sampling for 10 minutes during ultrasonic scaling	1. 0.05% CPC prior to scaling 2. 0.12% CHX prior to scaling Rinse duration: 1 minute	1. water PMR 2. no PMR	Bacterial load in CFUs (anaerobic culture), at 30 cm sampling distance. Also, samples for 39 oral/ periodontal bacterial species were analyzed using the

				checkerboard DNA-DNA hybridization technique (mean DNA % probe counts)
Fine et al, 1992 RCT, cross- over Setting: university	18 patients (ADA periodontal case type I, II); age: NR (adults); air sampling for 10 minutes during ultrasonic scaling	Antiseptic mouthwash (not-specified) PMR Rinse duration: 30 seconds	5% hydroalcochol control rinse	Bacterial load (aerobic culture) in CFUs, at 5 cm sampling distance
Gupta et al, 2014 RCT, parallel 3- arm Setting: university	24 patients (chronic periodontitis); age 25- 55; air sampling for 30 minutes during ultrasonic scaling plus 30 minutes thereafter	1. 0.2% CHX PMR 2. HRB PMR Rinse duration: 1 minute	Water PMR	Bacterial load (aerobic culture) in CFUs, at 30 cm sampling distance
Holloman et al, 2015 RCT, parallel 2- arm Setting: university	52 patients; age mean 45 (intervention group), mean 40 (control); air sampling (duration NR) during ultrasonic scaling, plus 35 minutes thereafter	Isolite (dental isolation system attached to high-volume suction hose)	Saliva ejector (attached to low-volume suction hose)	Bacterial load (anaerobic culture) in CFUs, at 15 cm sampling distance
Jawade et al, 2016 RCT, parallel 3- arm Setting; university	30 patients (chronic periodontitis); age 22- 55; air sampling for 20 minutes during ultrasonic scaling plus 20 minutes thereafter	1. Ultrasonic liquid coolant: 2% PI plus distilled water 2. Ultrasonic liquid coolant: 0.12% CHX plus distilled water	Distilled water (coolant)	Bacterial load (culture NR) in CFUs, at 40 cm to 2 m
Joshi et al, 2017 RCT, parallel 4- arm Setting: university	40 patients (chronic gingivitis); age mean 32.4; air sampling for 30 minutes during ultrasonic scaling plus 30 minutes thereafter	1. 0.05% CPC PMR (47°) 2. 0.2% CHX PMR (47°) Rinse duration: 1 minute	1. 0.05% CPC PMR (18°) 2. 0.2% CHX PMR (18°) Rinse duration: 1 minute	Bacterial load (aerobic culture) in CFUs, at 30 cm sampling distance

Kaur et al, 2014 RCT, parallel 3- arm Setting: university	60 patients; age 20- 50; air sampling for 10 minutes during ultrasonic scaling plus 30 minutes thereafter- both prior and after PMR	1. 0.2% CHX PMR 2. 1% PI PMR Rinse duration: NR	OZ irrigation	Bacterial load (aerobic and anaerobic culture) in CFUs, at 22- 275 cm sampling distance
King et al, 1997 RCT, split- mouth Setting: university	12 patients; age 21- 63 (mean 39); sampling for 5 minutes during ultrasonic scaling plus 25 minutes thereafter	Ultrasonic scaler with aerosol reduction device (ie, high volume suction tube attached to scaler)	Ultrasonic scaler without aerosol reduction device	Bacterial load (aerobic culture) in CFUs, at 15 cm sampling distance
Logothetis and Martinez- Welles, 1995 RCT, parallel 3- arm Setting: university	18 patients; age 25- 54, mean 38; sampling for 30 minutes during air polishing plus 30 minutes thereafter	1. 0.12% CHX PMR 2. Antiseptic mouthwash with essential oils PMR Rinse duration: 30 seconds	Distilled water Rinse duration: 30 seconds	Bacterial load (aerobic culture) in CFUs, at 60- 275 cm sampling distance
Mamajiwala et al, 2018 RCT, parallel 3- arm Setting: university	60 patients (moderate to severe gingivitis); age 15- 55; sampling for 20 minutes during ultrasonic scaling	1. CHX added in DUWL 2. CIN added in DUWL	Distilled water in DUWL	Bacterial load in CFUs (aerobic and anaerobic culture), within the range of 30 cm sampling distance
Mohan and Jagannathan, 2016 RCT, parallel 2- arm Setting: university	20 patients; age 25- 40; sampling during ultrasonic scaling/ duration NR	0.2% CHX PMR Rinse duration: 1 minute	Normal saline PMR Rinse duration: 1 minute	Bacterial load (culture NR) in CFUs, at 90 cm sampling distance
Narayana et al, 2016 nRS, parallel- 3 arm (plus within group control) Setting: NR	45 patients; age NR; air sampling during ultrasonic scaling for 5 minutes	1. 0.12% CHX PMR 2. HVE Rinse duration: 30 seconds	Combination of 0.12% CHX and HVE Rinse duration: 30 seconds	Bacterial load (aerobic culture) in CFUs, with blood agar plates and colony counters; sampling distance NR
Paul et al, 2020 nRS, parallel- 3 arm Setting: university	60 patients; age 18- 55 (mean 37.4, SD 10.3); air sampling during ultrasonic scaling for 20 minutes	1. 0.2% CHX PMR 2. 1% PI PMR Rinse duration: 1 minute	94.5% AV PMR Rinse duration: 1 minute	Bacterial load (aerobic culture) in CFUs, at 30 cm sampling distance

Purohit et al, 2009 nRS, parallel- 2 arm (plus within group control) Setting: university	20 patients; age NR; air sampling during a) ultrasonic scaling (oral prophylaxis) and b) tooth restoration through high-speed air turbine handpiece	1. Ultrasonic scaling with 0.12% CHX PMR 2. High speed air turbine tooth restoration with 0.12% CHX PMR Rinse duration: 30 seconds	1. Ultrasonic scaling without 0.12% CHX PMR 2. High speed air turbine tooth restoration without 0.12% CHX PMR Rinse duration: 30 seconds	Bacterial load (aerobic culture) in CFUs, at 15- 60 cm sampling distance
Rajachandrasekaran et al, 2019 nRS, parallel 2- arm Setting: university	50 patients; age 20- 50; air sampling during ultrasonic scaling for 30 minutes	0.12% CHX PMR Rinse duration: 1 minute	HRB PMR Rinse duration: 1 minute	Bacterial load (aerobic culture) in CFUs, at 60- 275 cm sampling distance (selective isolation of bacteria strains)
Rani et al, 2014 RCT, parallel 3- arm Setting: hospital	36 patients; age 18- 35; air sampling during ultrasonic scaling for 10 minutes	1. 0.2% CHX PMR 2. HRB PMR Rinse duration: 30 seconds	Water PMR Rinse duration: 30 seconds	Bacterial load (culture NR) in CFUs, at patient's and operator's chest (30 cm)
Reddy et al, 2012 RCT, parallel 3- arm Setting: hospital	30 patients; age NR; sampling during ultrasonic scaling/ duration NR	1. 0.2% tempered CHX (47^{O}C) PMR 2. 0.2% non-tempered CHX PMR Rinse duration: 1 minute	Sterile water PMR Rinse duration: 1 minute	Bacterial load (culture NR) in CFUs, at 10 cm sampling distance
Retamal- Valdes et al, 2017 RCT, parallel 4- arm Setting: dental office	60 patients; age 18- 70; sampling during ultrasonic scaling for 10 minutes	1. 0.075% CPC+ 0.28% Zn+ 0.05% SF PMR 2. 0.12 CHX PMR Rinse duration: 1 minute	1. Water PMR 2. No PMR Rinse duration: 1 minute	Bacterial load (anaerobic culture) in CFUs, at patient's chest and operator's forehand (15- 30 cm). Also, samples for oral/ periodontal bacterial species were analyzed using the checkerboard DNA-DNA hybridization technique (mean

				DNA % probe counts)
Saini et al, 2015 RCT, parallel 3- arm Setting: university	120 patients (chronic periodontitis); age 18- 55; sampling during ultrasonic scaling for 10 minutes- plus 30 pause, plus 10 after assignment to PMR	1. ClO_2 PMR 2. 0.2% CHX PMR Rinse duration: 1 minute	Water PMR Rinse duration: 1 minute	Bacterial load (culture NR) in CFUs, at 30- 245 cm sampling distance (mainly 30 cm)
Sawhney et al, 2015 RCT, parallel 3- arm parallel Setting: university	60 patients (mild to moderate gingivitis); age 25-54; sampling during ultrasonic scaling (duration NR)	1. CHX 0.2% PMR 2. Listerine PMR 3. Water PMR (all with suction) Rinse duration: 1 minute	1. CHX 0.2% PMR 2. Listerine PMR 3. Water PMR (all without suction) Rinse duration: 1 minute	Distribution of microbial growth in percentages, at sampling distance 15 cm
Sethi et al, 2019 RCT, parallel 3- arm Setting: university	60 patients (moderate to severe gingivitis); age 18- 55 (mean 29.26; SD, 2.8); sampling during ultrasonic scaling for 20 minutes	1. CHX as ultrasonic coolant 2. CIN PMR as ultrasonic coolant	Distilled water as ultrasonic coolant	Bacterial load (aerobic culture) in CFUs, at 30 cm sampling distance
Shetty et al, 2013 RCT, parallel 3- arm Setting: university	60 patients; age NR; sampling during ultrasonic scaling for 10 minutes	1. 0.2% CHX PMR 2. Tea tree oil PMR Rinse duration: NR	Distilled water Rinse duration: NR	Bacterial load (aerobic culture) in CFUs, at 15- 30 cm
Swaminathan et al, 2014 RCT, parallel 3- arm Setting: university	30 patients; age 18- 50; sampling during ultrasonic scaling for 30 minutes	1. 0.2% CHX PMR 2. HRB PMR Rinse duration: 1 minute	Normal Saline PMR Rinse duration: 1 minute	Bacterial load (aerobic culture) in CFUs, at 30- 90 cm sampling distance
Toroglou et al, 2001 nRS, parallel- 2 arm (plus within group control) Setting: NR	26 patients; age intervention group 11- 13; age control group 10-15; sampling during orthodontic	Debonding/ adhesive removal, through the use of an air turbine handpiece, with water cooling	Standard orthodontic procedures that did not require turbine handpiece, with	Bacterial load (aerobic culture) in CFUs, at or less than 30 cm sampling distance; also specific tests for Staphylococcus,

	debonding procedures (5 minutes working time, plus 25 minutes thereafter)	and slow speed evacuation (0.2% CHX as within group control) Rinse duration: 1 minute	slow speed evacuator	Streptococcus and oxidase activity
Waghmare et al, 2018 RCT, parallel 3- arm Setting: NR	60 patients; age 20- 28; sampling during ultrasonic scaling for 30 minutes	1. 1% ClO_2 PMR 2. 0.2% CHX PMR Rinse duration: 1 minute	Normal Saline PMR Rinse duration: 1 minute	Bacterial load (aerobic culture) in CFUs, at 30 cm sampling distance
NCT02319668 GlaxoSmithKline, 2017 RCT, parallel 2- arm Setting: NR	38 patients; age 18- 64, mean 27.9, SD 10.5; sampling during dental prophylaxis (not- specified procedure)	0.2% CHX PMR Rinse duration: 1 minute	No PMR	Bacterial load (anaerobic culture) in CFUs, at certain positions around dental unit

AV, aloe vera; CFUs, colony forming units; CHX, chlorhexidine; CIN, cinnamon; ClO2, chlorine dioxide; CPC, cetylpiridinium chloride; DGGE, denaturing gradient gel electrophoresis; DUWL, dental unit waterline; HRB: herbal mouthwash; HVE, high volume evacuator; NR, not reported; nRS, non- randomized prospective studies; OZ, ozone; PCR, polymerase chain reaction; PMR, pre-procedural mouth rinse; PI, povidone iodine; SD, standard deviation; SF, sodium fluoride; Zn, zinc lactate

Table 2. League table, indicating network meta-analysis (NMA) mean differences in log_{10} CFUs (colony forming units), below the diagonal. Comparisons are indicated by the column vs the row defining the intervention prior to ultrasonic scaling. Negative (-) mean differences are in favor of the column presented interventions, indicating reduced pathogen load. Direct meta-analysis results are presented above the diagonal in a similar manner. Mean differences for comparisons in the opposite direction may be obtained through conversion of negative to positive values and vice versa.

CHX 0.12%		0.50 (-0.66, 1.66)					0.03 (-1.01, 1.08)		
0.31 (-0.83, 1.45)	temp. CHX 0.2%	0.93 (0.01, 1.85)					0.17 (-0.80, 1.14)		0.21 (-0.42, 0.84)
-0.60 (-1.65, 0.44)	-0.92 (-1.54, -0.29)	Control			-0.31 (-0.89, 0.27)	-0.28 (-1.25, 0.68)	-0.47 (-1.66, 0.72)	-0.62 (-1.13, -0.11)	-0.84 (-1.00, -0.68)
-0.11 (-1.72, 1.50)	-0.42 (-1.77, 0.93)	0.50 (-0.76, 1.75)	PI	-0.22 (-1.25, 0.81)					-0.24 (-1.41, 0.93)
0.11 (-1.40, 1.63)	-0.20 (-1.44, 1.03)	0.72 (-0.42, 1.85)	0.22 (-0.85, 1.29)	OZ					-0.02 (-1.06, 1.02)
-0.29 (-1.49, 0.91)	-0.61 (-1.47, 0.25)	0.31 (-0.28, 0.90)	-0.18 (-1.57, 1.20)	-0.40 (-1.68, 0.87)	HVE				
-0.14 (-1.46, 1.19)	-0.45 (-1.46, 0.56)	0.47 (-0.38, 1.31)	-0.03 (-1.50, 1.45)	-0.25 (-1.62, 1.12)	0.16 (-0.87, 1.19)	HRB			-0.13 (-1.04, 0.79)
0.04 (-0.95, 1.03)	-0.27 (-1.09, 0.54)	0.64 (-0.12, 1.40)	0.15 (-1.28, 1.57)	-0.07 (-1.39, 1.25)	0.33 (-0.63, 1.30)	0.18 (-0.93, 1.28)	CPC		-0.01 (-0.98, 0.96)
0.07 (-1.00, 1.15)	-0.24 (-0.88, 0.39)	0.68 (0.34, 1.01)	0.18 (-1.06, 1.42)	-0.04 (-1.16, 1.08)	0.37 (-0.31, 1.04)	0.21 (-0.66, 1.07)	0.03 (-0.75, 0.81)	ClO_2	-0.08 (-0.20, 0.03)
0.13 (-0.93, 1.19)	-0.18 (-0.78, 0.41)	0.74 (0.40, 1.07)	0.24 (-0.97, 1.45)	0.02 (-1.06, 1.10)	0.42 (-0.25, 1.10)	0.27 (-0.57, 1.11)	0.09 (-0.66, 0.84)	0.06 (-0.21, 0.33)	CHX 0.2%

FIGURES

Figure 1.

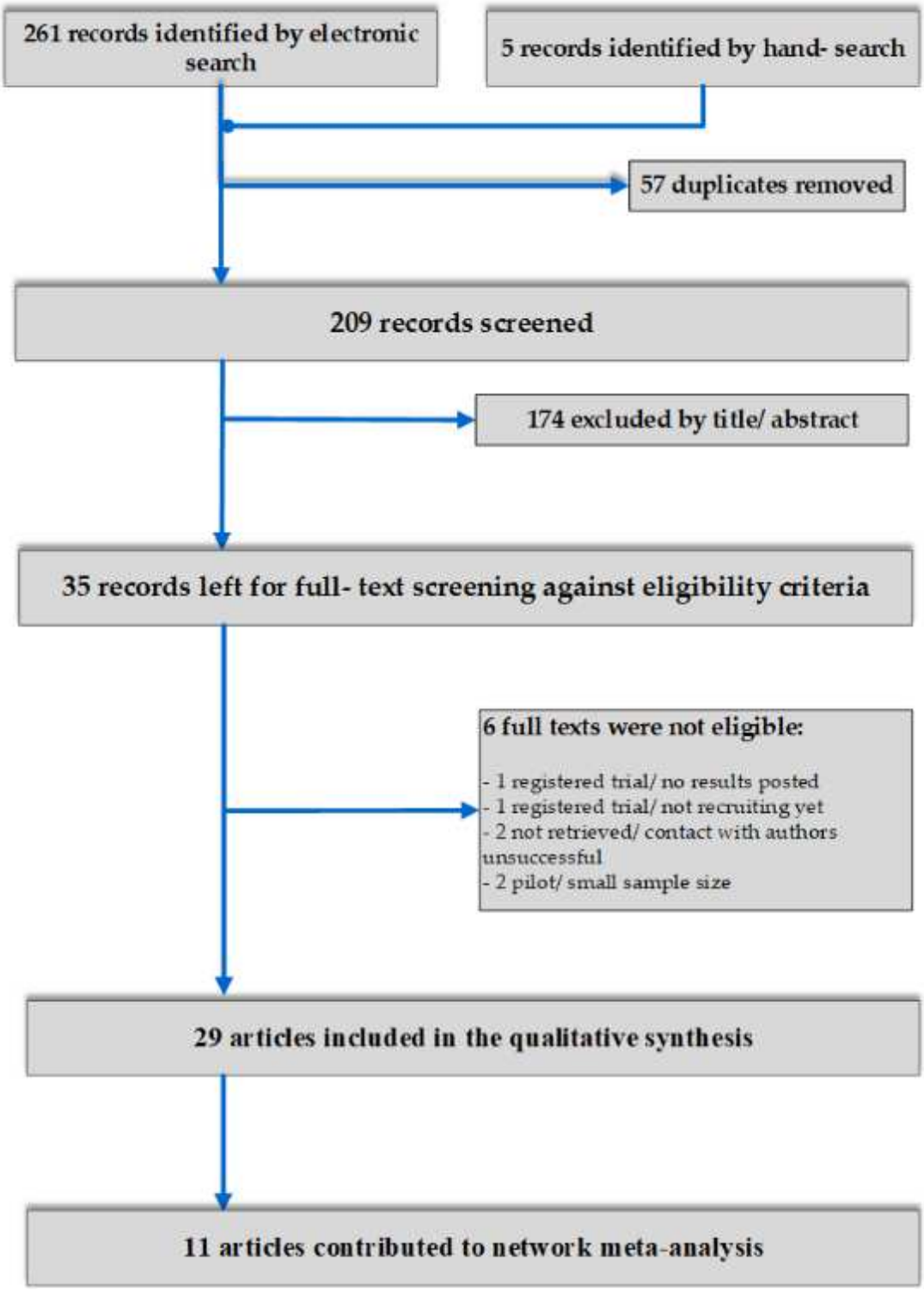

Figure 2.

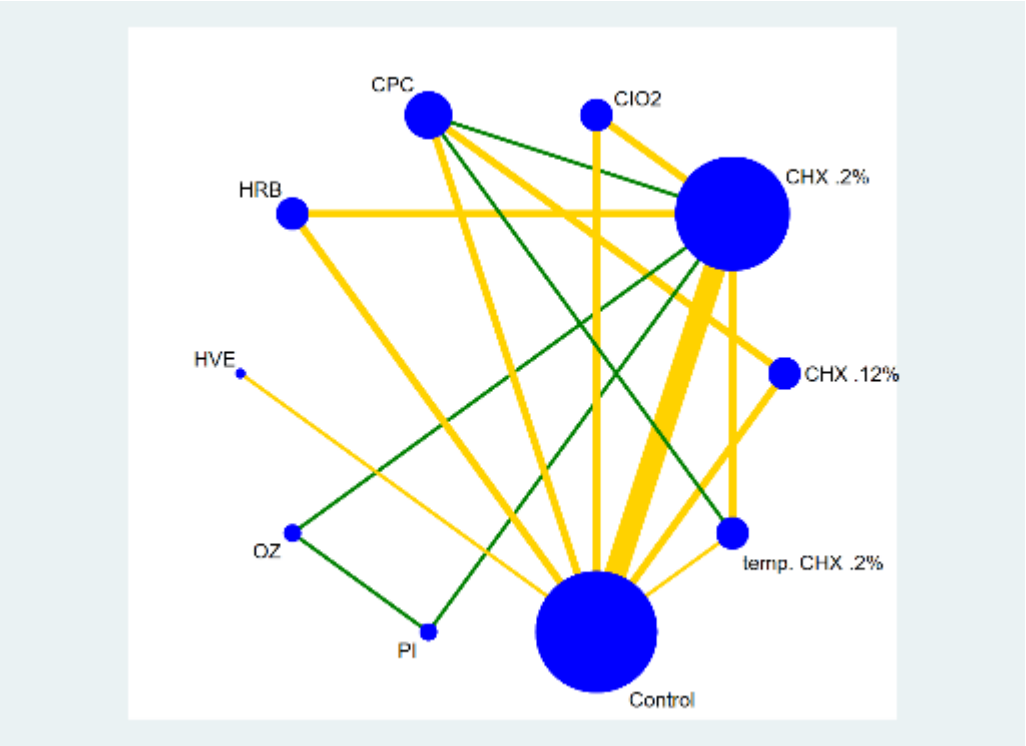

Figure 3.

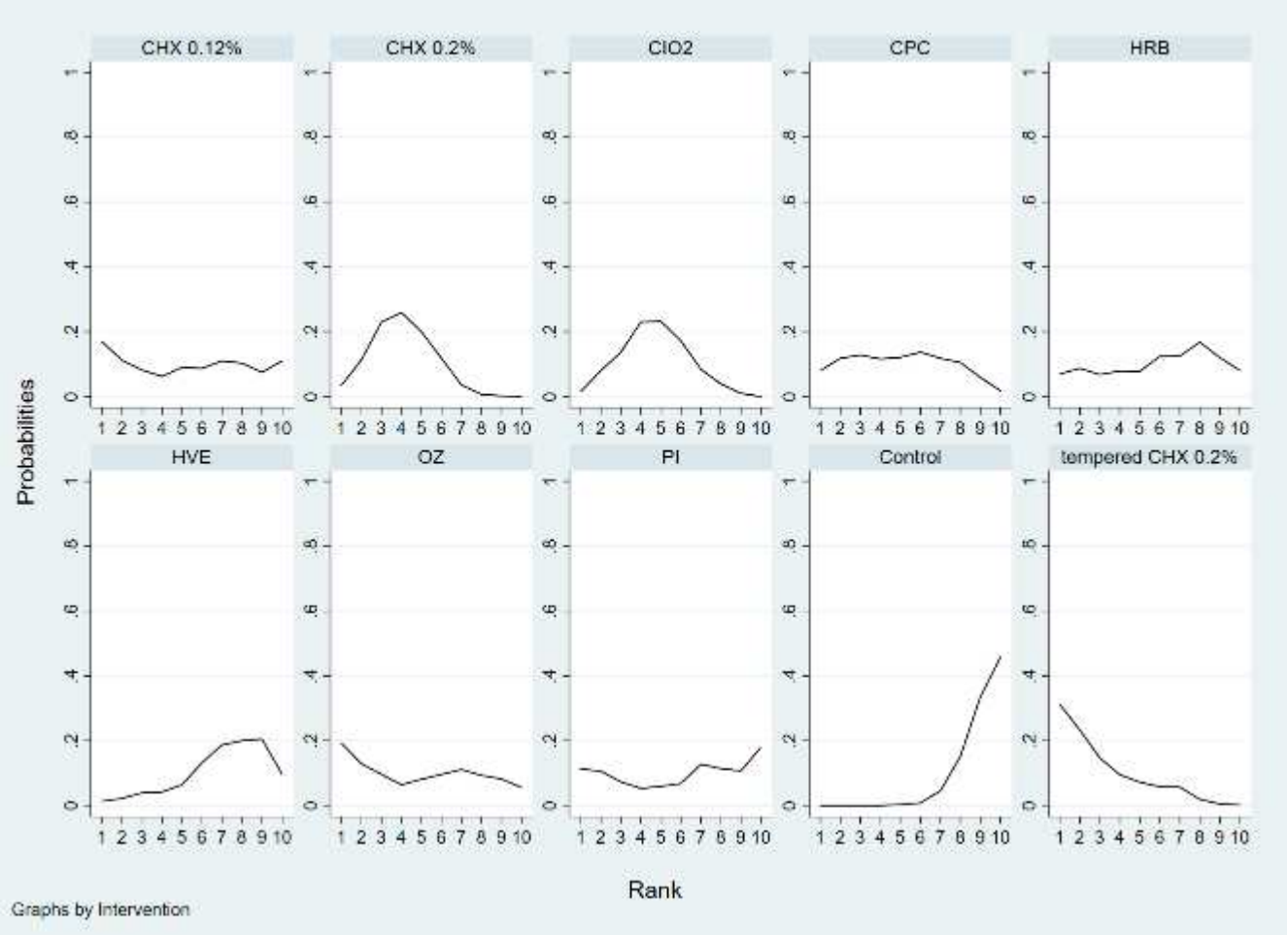
CHX 0.12%
CHX 0.2%
ClO2
CPC
HRB
HVE
OZ
PI
Control
tempered CHX 0.2%
Probabilities
Rank
Graphs by Intervention

Figure 4.

Comparison (No.Studies)	Within study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
Mixed evidence							
CHX .2% vs ClO2 (2)							Low
CHX .2% vs Control (6)							Moderate
CHX .2% vs OZ (1)							Very Low
CHX .2% vs temp.CHX .2% (2)							Low
ClO2 vs Control (2)							Moderate
Control vs temp.CHX .2% (1)							Moderate
Indirect evidence							
ClO2 vs OZ							Very Low
ClO2 vs temp.CHX .2%							Low
Control vs OZ							Low
OZ vs temp.CHX .2%							Very Low

No concerns/Undetected bias
Some concerns
Major concerns

Appendix Text

Methodology

Data Collection

Data extraction was employed in pre- piloted standardized forms by one independently working reviewer (DK) and confirmed by a second (TE). Specifically, information entries related to study design, sample size, population, intervention, comparator, and outcomes.

Risk of bias in individual studies

Risk of bias assessment was performed independently by one author (DK) and all recordings were confirmed by a second (TE). Any disagreements were settled after consultation with a third author (GNB). For the randomized controlled trials (Koletsi et al. 2012; Koletsi et al. 2016), the updated Cochrane RoB 2.0 tool was used (Sterne et al. 2019). For non- randomized prospective clinical trials, the ROBINS-I tool was used, accordingly (Sterne et al. 2016).

Summary measures and Data syntheses

Clinical heterogeneity was examined first, in terms of individual study settings and conditions, population characteristics, eligibility criteria or methods of analyses and also outcomes. If possible, statistical heterogeneity was planned to be examined, first visually, through inspection of the confidence bounds within the forest plots, second statistically, as indicated by a P- value below the level of 10% for the test ($p<0.10$). I^2 test for homogeneity was also undertaken for pairwise comparisons (Higgins et al. 2003).

For the network of meta-analysis planned, only randomized controlled trials were included in the quantitative synthesis across different comparisons (mixed/ direct/ indirect), in an attempt to minimize bias. Random- effects meta- analyses with restricted maximum likelihood estimators were employed, as they were considered more appropriate to incorporate individual study settings, if possible. As continuous outcome(s) were anticipated, treatment effects were calculated through pooled mean differences (MD) with associated 95% Confidence Intervals (95% CIs). Outcome values were transformed (in $\log_{10}$ scale) where needed to achieve consistency between measured interventions across all studies. A set of network estimates for all comparisons were constructed and the amount of inconsistency was checked through a closed loop of evidence (Veroniki et al. 2013). In addition, inconsistency between direct and indirect evidence was checked through the

node- splitting model as originally proposed from Dias et al (Dias et al. 2010) and modified by White in 2015 (White 2015). To this respect, potential effect modifiers were examined (ie, different populations, types of pathogen analyses) in an attempt to assess their capacity to induce intransitivity (Salanti 2012). An overall rank score of the effectiveness of each intervention was employed, in line with the surface under the curve cumulative ranking (SUCRA) value (Chaimani et al. 2013). Relative rankings for the competing treatments were presented through ranking probabilities for each identified outcome. The SUCRA values represent the surface under the curve ("surface under cumulative ranking"). A high SUCRA value corresponds to an intervention with high probabilities of being in the first ranks of treatment of choice.

Assessment of the Quality of the Evidence and Assessment of Confidence in the Estimated Effect

For the interventions and comparisons of the network, the novel CINeMA framework was used (Nikolakopoulou et al. 2020; Papakonstantinou et al. 2020), which is based on the original GRADE tool (Guyatt et al. 2008), but expanded for assessment of the level of confidence stemming from the results of network meta-analysis. Allied with GRADE, the overall body of evidence is rated as high, moderate, low and very low. The ratings, with regard to the likelihood for a change in our confidence in the estimated effect, range from very unlikely to very likely to be modified. In addition, when the overall quality of the body of evidence is rated as very low, then any estimated effect is particularly uncertain. Assessment of the body of evidence primarily entails identification of study design. In terms of randomized designs, which present a theoretically 'high' quality of the evidence, assessment is made following the 6 domains that are considered to affect the level of confidence: 1. Within study bias, 2. Reporting bias, 3. Indirectness, 4. Imprecision, 5. Heterogeneity and 6. Incoherence. From each comparison of the network, the level of concern is established, ie, "no concern", "some concern", "major concern", giving feed-up to the final confidence rating, as "high", "moderate", "low", or "very low". Only the most relevant comparisons, between the four treatments with the highest SUCRA value were considered, as well as the non- active control treatment.

Risk of Bias across studies

Publication bias was examined through a comparison adjusted funnel plot, which included all network contributors, according to Chaimani et al, 2013 (Chaimani et al. 2013).

Additional analyses

Sensitivity analyses were planned, to explore and isolate the effect of potentially different populations across studies (ie, patients with periodontal disease).

Results

Study Descriptive Data

The most common dental procedure examined was ultrasonic scaling (24/ 29; 82.8%), while 2 studies reported on outcomes after debonding procedures of orthodontic fixed appliances (Toroglu et al. 2001; Dawson et al. 2016), air- polishing (Logothetis and Martinez-Welles 1995), tooth restoration through with the use of high- speed air turbine (Purohit et al. 2009) and other dental prophylaxis procedures without instrumentation justification (NCT02319668). All studies pertained roughly to the assessment of bacterial load colony forming units (CFUs) after the application of a number of interventions prior or simultaneously to a commonly described dental procedure, namely, as aforementioned, ultrasonic scaling, but also enamel clean- up after debonding procedures, or tooth restoration. In essence, blood agar plates were used across the studies to collect the aerosolized bacteria, while subsequently aerobically and/ or anaerobically incubated and analyzed in colony counters. The sampling distance ranged between 5 and 275 cm, away from patients' oral cavity, with the majority of trials investigating close- up distances, such as patient's thoracic region, clinician's face, or specific targets around the dental unit, where the presence of clinic staff might be at stake. These targets were within the range of 15 to 90 cm. Interestingly, only two studies reported on additional specification of bacterial species, via checkerboard DNA- DNA hybridization techniques, measuring mean percentage DNA probe counts (Feres et al. 2010; Retamal-Valdes et al. 2017). Yet, these included primarily oral/periodontal microbes, rather than species that may cause non-oral opportunistic infections. Air sampling across studies pertained to a duration of 5 minutes in the course of the dental procedure until 35 minutes after its completion. The variety of the reported interventions in the included studies, irrespective of the dental procedure implemented in practice were as follows: pre- procedural mouthrinse (PMR) with chlorhexidine (CHX) 0.2%, 0.12% or tempered CHX 0.2%, cetylpiridinium chloride PMR (CPC) 0.05%, use of high volume evacuator (HVE) jointly with CHX or alone, ultrasonic scaler with high- volume suction tube attached, herbal PMR (ie, oil tree, aloe vera), ozone (OZ), povidone iodine PMR (PI), CHX 0.12% or PI used as ultrasonic coolants, CHX or cinnamon (CIN) used in dental unit waterlines (DUWLs), chlorine dioxide (ClO_2), as well as control non- active interventions such as water, distilled

water, normal saline, simple saliva ejector, or no PMR at all. For the interventions that pertained to PMR solutions, the duration was 30 seconds to 2 minutes (Table 1).

Risk of bias within studies

The internal validity of the included studies ranged from moderate to serious risk of bias for the non- randomized prospective trials (Appendix Table 2a, 2b), while with regard to their randomized counterparts, the ratings varied from low to high risk of bias (Appendix Table 3a, 3b). In essence, the former study design comprised of a preponderance of serious risk of bias studies (6 out of 8), while for the latter design (RCTs), 6 studies were rated as low risk of bias, one as high, and the rest (14/ 21) were considered as pertaining to "some concerns" regarding their validity. A close breakdown to non- randomized studies characterized as serious risk of bias, revealed confounding and issues related to measurement of the outcome as being the most inadequately handled by the authors of these studies, at least at the level of reporting (Appendix Table 2a, 2b). For the RCTs, randomization scheme issues, with allocation concealment frequently inadequately reported, or potential lack of blinding of outcome assessors, were the most severely affected parameters (Appendix Table 3a, 3b). A notable category of a special type of bias- related effect was also observed, which pertained to inter- group contamination or, in split- mouth or cross overs study designs, although not considerably prevalent in our sample cohort (6/ 29; 20.6%).

In terms of RCTs that contributed to the network of interventions being studied, all comparisons were at most of "some concerns", with none presenting high risk of bias. In particular, five comparisons with 5 implicated interventions were recorded as low risk of bias. These were the tempered chlorhexidine (CHX) .2% compared to cetylpiridinium chloride (CPC), CPC compared to CHX .2%, ozone (OZ) compared to povidone iodine (PI), as well as the two latter compared to CHX .2% respectively. All other comparisons were rated as of presenting "some concerns", which practically means that at least one contributing study to the comparison of interest was rated as originally presenting "some concerns" (Figure 2). In essence and with regard to the identified most effective intervention, namely the tempered CHX .2%, one of the included studies demonstrated low risk of bias (Joshi et al. 2017) and another one "some concerns" (Reddy et al. 2012). The contribution of within study bias to the overall framing of the quality and the confidence of the retrieved evidence is also provided through the CINeMA framework approach (Figure 4).

Single study findings

As for single study estimates from both randomized and non- randomized trials, regarding aerosol reducing intervention strategies for alternate dental procedures, use of solutions as ultrasonic scaler coolants, as extracts for the DUWLs, air-polishing practices, or enamel clean- up after fixed appliance orthodontic treatment have been described (Appendix Table 5). Specifically, CHX in concentration of either 0.12% or 0.2%, CIN, or PI have been reported as significantly effective strategies when used as ultrasonic coolants, compared to control water use ($p<0.001$). Similar findings were confirmed for CHX and CIN, when used as DUWL extracts ($p<0.001$). In addition, CHX 0.12% as PMR was more effective than HRB related solution, when used prior to air- polishing procedures ($p<0.001$). Last, with regard to potentially hazardous diverse dental procedures routinely used, tooth restoration activities with high- speed handpiece were considered more "aerosol pathogen inductive" than ultrasonic scaling ($p<0.001$); however, this effect was eliminated after PMR with CHX 0.12%. Likewise, debonding and enamel clean- up activities in orthodontic practices were more prone to producing contaminated aerosols than routine orthodontic practices ($p=0.001$) (Appendix Table 5).

Additional Analyses

A sensitivity analysis to explore the potential effect of specific populations such as periodontal patients was conducted, as pre- specified, and as an adjunct to the exploration for effect modification. As such, we examined the network backbone after excluding two studies (Gupta et al. 2014; Saini 2015), involving chronic periodontitis patients. The results of the sensitivity network meta- analysis are shown in Appendix Table 6 and appear in line with those of the main synthesis. When considering ranking of the effectiveness of the competing interventions, the tempered CHX 0.2% ranked first, both in the overall SUCRA value (78.8%), as well as in the probability of being the treatment of choice (probability best, 28.8%).

Risk of bias across studies

Evidence of publication bias or small study effects could not be confirmed after inspection of the comparison adjusted funnel plot for the aerosol bacterial load network (Appendix Figure 6).

Discussion

Relation of identified interventions to SARS-CoV-2 management

Unlike chlorhexidine, PI, OZ and ClO_2 might be perceived as additionally effective germicides related to certain pathogen types, due to their oxidation potential in reaction with microbial or virus cell structure (Yoo 2018). However, latest FDA release announcements have been particularly critical and alarming against the use of ClO_2 products for disease prevention and treatment, including the novel coronavirus disease 2019 (COVID-19) (FDA news release 2020 Apr 9). Ozone applications in dentistry have been identified and emerged as promising adjuncts to scaling and root planning in periodontal therapy, either as gaseous compounds or as irrigating substances, but with questionable outcomes (Seydanur Dengizek et al. 2019). To this end, the findings of the present review, although identifying OZ as an agent with high probabilities of being effective against aerosolized bacteria, indicate a questionable level of confidence to the effect of OZ, raising issues related to within- study bias and imprecision of the estimated effect. Pre- procedural mouthrinse with Povidone Iodine 1% (PI) ranked 4^{th} in terms of probabilities of best treatment of choice for effectiveness related to aerosolized bacteria, according to the present NMA, preceded by chlorhexidine solutions and ozone. Currently, PI (0.2% to 1%) has emerged together with an alternative oxidative agent, namely the hydrogen peroxide 1% (H_2O_2), as prescription solutions, for mouthwash use in dental practice for the management of SARS-CoV-2 diffusion, by two reports (Peng et al. 2020; Izzetti et al. 2020). Both related reports are based on the initial guidance for diagnosis and treatment of novel coronavirus disease 2019, released by the National Health Commission by the People's Republic of China, regarding potential ineffectiveness of CHX against the virus (National Health Commission PRC 2020). There is currently no evidence from clinical trials or relative effectiveness compared to competing interventions, on aerosolized or airborne viral load in dental practice after the use of PI or H_2O_2. However, their use may be reasonable, pertaining to their oxidation potential on viral load in saliva and subsequently in aerosolized compounds of saliva, blood and pathogen following routine dental procedures, especially those implicating high-speed handpiece air- turbine use. Inductively, the same goes for the novel SARS-CoV-2. With special interest on PI and implications on its effect on the novel SARS-CoV-2, literature reveals that PI bears the capacity to gradually and slowly release iodine on the lipid shell and the lipid membrane viral pathogens. Resulting advantage is two- fold: first, lipid shell membrane is destroyed and oxidation of the cellular components renders the virus inactive; second, toxicity and adverse effects are minimized by slow iodine release (Yoo 2018). Up to date, application of H_2O_2 and research in dentistry has been confined to the study of peroxide as mouthwash on the prevention of plaque and gingival inflammation (Hossainian et al. 2011), but mainly as DUWL disinfectant agent, with

reported effectiveness in reducing activity of bacterial biofilms within the waterlines (Ditommaso et al. 2016). A pilot study in 2015, reported the use of 1.5% H_2O_2 as a topical agent prior to CHX rinse for pre- procedural ultrasonic scaling and yielded promising results in terms of bacterial reduction in generated aerosol (Ramesh et al. 2015). In addition, calls for the launch of clinical trials to test the effectiveness of flavonoids and/ or cyclodextrins against the SARS-CoV-2 viral load in saliva or aerosol expectorations have lately emerged (Carrouel et al. 2020).

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Appendix Table 1. Electronic Database Search

No.	Electronic Database	Hits
1.	**Medline via Pubmed** ((aerosol) OR (splatter) OR (aerosols) OR (airborne) OR (bioaerosol) OR (bioaerosols) OR (spatter) OR (droplet) OR (droplets)) AND ((dental practice) OR (dental procedure) OR (ultrasonic dental scaling) OR (ultrasonic dental) OR (ultrasonic dental unit) OR (tooth grinding) OR (tooth restoration) OR (tooth scaling) OR (teeth scaling) OR (teeth grinding) OR (rotary dental instruments) OR (bracket debonding) OR (orthodontic debonding) OR (composite removal) OR (resin removal) OR (adhesive removal) OR (dental unit waterline) OR (DUWL)) AND ((bacterial load) OR (bacterial count) OR (microbial load) OR (microbial count) OR (bacterial colony) OR (microbial colony) OR (virus) OR (viral) OR (microbe))	**93**
2.	**Scopus** *(TITLE-ABS* *KEY (((aerosol) OR (splatter) OR (aerosols) OR (airborne) OR (bioaerosol) OR (bioaerosols) OR (spatter) OR (droplet) OR (droplets)))) AND (TITLE-ABS-* *KEY (((bacterial AND load) OR (bacterial AND count) OR (microbial AND load) OR (microbial AND count) OR (bacterial AND colony) OR (microbial AND colony) OR (virus) OR (viral) OR (microbe)))) AND (TITLE-ABS-* *KEY (((dental AND practice) OR (dental AND procedure) OR (ultrasonic AND dental AND scaling) OR (ultrasonic AND dental) OR (ultrasonic AND dental AND unit) OR (tooth AND grinding) OR (tooth AND restoration) OR (tooth AND scaling) OR (teeth AND scaling) OR (teeth AND grinding) OR (rotary AND dental AND instruments))))	**135**
3.	**Cochrane Central Register of Controlled Trials (CENTRAL)** ((aerosol) OR (splatter) OR (aerosols) OR (airborne) OR (bioaerosol) OR (bioaerosols) OR (spatter) OR (droplet) OR (droplets)) AND ((dental practice) OR (dental procedure) OR (ultrasonic dental scaling) OR (ultrasonic dental) OR (ultrasonic dental unit) OR (tooth grinding) OR (tooth restoration) OR (tooth scaling) OR (teeth scaling) OR (teeth grinding) OR (rotary dental	**23**

	instruments) OR (bracket debonding) OR (orthodontic debonding) OR (composite removal) OR (resin removal) OR (adhesive removal) OR (dental unit waterline) OR (DUWL)) AND ((bacterial load) OR (bacterial count) OR (microbial load) OR (microbial count) OR (bacterial colony) OR (microbial colony) OR (virus) OR (viral) OR (microbe))	
4.	**Cochrane Database of Systematic Reviews (CDSR)** ((aerosol) OR (splatter) OR (aerosols) OR (airborne) OR (bioaerosol) OR (bioaerosols) OR (spatter) OR (droplet) OR (droplets)) AND ((dental practice) OR (dental procedure) OR (ultrasonic dental scaling) OR (ultrasonic dental) OR (ultrasonic dental unit) OR (tooth grinding) OR (tooth restoration) OR (tooth scaling) OR (teeth scaling) OR (teeth grinding) OR (rotary dental instruments) OR (bracket debonding) OR (orthodontic debonding) OR (composite removal) OR (resin removal) OR (adhesive removal) OR (dental unit waterline) OR (DUWL)) AND ((bacterial load) OR (bacterial count) OR (microbial load) OR (microbial count) OR (bacterial colony) OR (microbial colony) OR (virus) OR (viral) OR (microbe))	**0**
5.	**Open Grey** (aerosol) AND (dental) (aerosol) AND (ultrasonic)	**1** **6**
6.	**ClinicalTrials.gov (**www.clinicaltrials.gov**)** (aerosol) AND (dental) (aerosol) AND (ultrasonic)	**1** **2**
7.	**National Research Register (ISRCTN:** www.controlled-trials.com**)** (aerosol) AND (dental) (aerosol) AND (ultrasonic)	**0** **0**

Appendix Table 2a. Risk of Bias assessment for non- randomized studies (ROBINS-I).

	Bias due to / in…							
Study	**Confounding**	**Selection of participants into the study**	**Classification of interventions**	**Deviations from intended interventions**	**Missing data**	**Measurement of outcomes**	**Selection of the reported result**	**Overall**
Dawson et al, 2016	**Low**	**Low**	**Low**	**Low**	**Low**	**Moderate**	**Moderate**	**Moderate**
Devker et al, 2012	**Serious**	**Low**	**Low**	**Low**	**No Information**	**Moderate**	**No Information**	**Serious**
dos Santos et al, 2014	**Low**	**Low**	**Low**	**Low**	**Low**	**Moderate**	**Moderate**	**Moderate**
Narayana et al, 2016	**Serious**	**Low**	**Low**	**Low**	**No Information**	**Moderate**	**No Information**	**Serious**
Paul et al, 2020	**Serious**	**Low**	**Low**	**Low**	**No Information**	**Moderate**	**No Information**	**Serious**
Purohit et al, 2009	**Serious**	**Low**	**Moderate**	**Low**	**No Information**	**Moderate**	**No Information**	**Serious**
Rajachandrasekaran et al, 2019	**Serious**	**Low**	**Moderate**	**Low**	**No Information**	**Moderate**	**No Information**	**Serious**
Toroglou et al, 2001	**Serious**	**Low**	**Moderate**	**Low**	**No Information**	**Low**	**No Information**	**Serious**

Appendix Table 2b. Detailed assessment of ROBINS-I.

Domain	Reference	Dawson et al, 2016	Devker et al, 2012	Dos Santos et al, 2014	Narayana et al, 2016	Paul et al, 2020	Purohit et al, 2009	Rajachandrasekaran et al, 2019	Toroglou et al, 2001
1. Confounding	1.1	N	PY	N	PY	PY	PY	PY	PY
	1.2	NA	N	NA	N	N	N	N	N
	1.3	NA	NA	NA	NA	NA	NA	NA	NA
	1.4	NA	PN	NA	PN	PN	PN	PN	PN
	1.5	NA	NA	NA	NA	NA	NA	NA	NA
	1.6	NA	PN	NA	PN	PN	PN	PN	PN
	1.7	NA	PN	NA	PN	PN	PN	PN	PN
	1.8	NA	NA	NA	NA	NA	NA	NA	NA
	Judgement	Low	Serious	Low	Serious	Serious	Serious	Serious	Serious
2. Selection of participants into the study	2.1	N	N	N	N	N	PN	PN	PN
	2.2	NA	NA	NA	NA	NA	NA	NA	NA
	2.3	NA	NA	NA	NA	NA	NA	NA	NA
	2.4	Y	Y	Y	PY	PY	PY	PY	PY
	2.5	NA	NA	NA	NA	NA	NA	NA	NA
	Judgement	Low	Low	Low	Low	Low	Low	Low	Low
3. Classification of interventions	3.1	Y	Y	Y	Y	Y	Y	Y	Y
	3.2	Y	Y	Y	Y	Y	Y	Y	Y
	3.3	PN	PN	PN	PN	PN	PY	PY	PY
	Judgement	Low	Low	Low	Low	Low	Moderate	Moderate	Moderate
4. Deviations from intended interventions	4.1	N	N	N	N	N	PN	PN	PN
	4.2	NA	NA	NA	NA	NA	NA	NA	NA
	4.3	NA	NA	NA	NA	NA	NA	NA	NA
	4.4	NA	NA	NA	NA	NA	NA	NA	NA
	4.5	NA	NA	NA	NA	NA	NA	NA	NA
	4.6	NA	NA	NA	NA	NA	NA	NA	NA
	Judgement	Low	Low	Low	Low	Low	Low	Low	Low
5. Missing data	5.1	Y	NI	PY	NI	NI	NI	NI	NI
	5.2	N	NI	PN	NI	NI	NI	NI	NI
	5.3	N	NI	PN	NI	NI	NI	NI	NI
	5.4	NA	NA	NA	NA	NA	NA	NA	NA

	5.5	NA	NA	NA	NA	NA	NA	NA	NA
	Judgement	Low	No Information	Low	No Information	No information	No Information	No information	No Information
6. Measurement of outcomes	6.1	PN	PN	PN	PN	PN	PY	PY	PY
	6.2	NI	NI	NI	NI	NI	NI	NI	N
	6.3	Y	Y	Y	Y	Y	Y	Y	Y
	6.4	PN	PN	PN	PN	PN	PN	PN	PN
	Judgement	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Low
7. Selection of the reported result	7.1	NI	NI	NI	NI	NI	NI	NI	NI
	7.2	NI	NI	NI	NI	NI	NI	NI	NI
	7.3	PN	NI	PN	NI	NI	NI	NI	NI
	Judgement	Moderate	No Information	Moderate	No Information	No Information	No Information	No information	No Information
Overall	Judgement	Moderate	Serious	Moderate	Serious	Serious	Serious	Serious	Serious
Note		Small number of patients							

Y, yes; PY, probably yes; N, no; PN, probably no; NI, no information; NA, not applicable

Appendix Table 3a. Risk of bias of included randomized clinical trial with the RoB 2.0 tool.

Study	Randomization	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Feres et al, 2010	**Some concerns**	**Low**	**Low**	**Low**	**Low**	**Some concerns**
Fine et al, 1992	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Gupta et al, 2014	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Holloman et al, 2015	**Some concerns**	**Low**	**Low**	**Low**	**Low**	**Some concerns**
Jawade et al, 2016	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Joshi et al, 2017	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Kaur et al, 2014	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
King et al, 1997	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Logothetis and Martinez- Welles, 1995	**Some concerns**	**Low**	**Low**	**Low**	**Low**	**Some concerns**
Mamajiwala et al, 2018	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Mohan and Jagannathan, 2016	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Rani et al, 2014	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Reddy et al, 2012	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Retamal- Valdes et al, 2017	**Low**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Saini 2015	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Sawhney et al, 2015	**Some concerns**	**Some concerns**	**Low**	**Some concerns**	**Low**	**Some concerns**
Sethi et al, 2019	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Shetty et al, 2013	**Some concerns**	**Low**	**Low**	**Low**	**Low**	**Some concerns**
Swaminathan et al, 2014	**Some concerns**	**Low**	**Low**	**Some concerns**	**Low**	**Some concerns**
Waghamare et al, 2018	**Some concerns**	**Low**	**Low**	**Low**	**Low**	**Some concerns**
NCT02319668	**Some concerns**	**Low**	**Low**	**High**	**Low**	**High**

Appendix Table 3b. Detailed assessment of RoB 2.0 tool.

Domain	Reference	Feres et al, 2010	Fine et al, 1992	Gupta et al, 2014	Holloman et al, 2015	Jawade et al, 2016	Joshi et al, 2017	Kaur et al, 2014	King et al, 1997
1. Randomization process	1.1	PY	Y	PY	PY	PY	Y	PY	PY
	1.2	NI	Y	Y	NI	NI	Y	PY	NI
	1.3	PN	N	PN	PN	PN	N	PN	PN
	Assessor's Judgement	Some concerns	Low	Low	Some concerns	Some concerns	Low	Low	Some concerns
2. Deviations from intended interventions	2.1	Y	N	N	PY	NI	PN	N	PY
	2.2	N	N	N	Y	NI	N	N	PY
	2.3	PN	NA	NA	PN	PN	NA	NA	PN
	2.4	NA	NA	NA	NA	NA	NA	NA	NA
	2.5	NA	NA	NA	NA	NA	NA	NA	NA
	2.6	PY	PY	PY	PY	PY	PY	PY	PY
	2.7	NA	NA	NA	NA	NA	NA	NA	NA
	Assessor's Judgement	Low	Low	Low	Low	Low	Low	Low	Low
3. Mising outcome data	3.1	PY	PY	Y	Y	PY	Y	PY	Y
	3.2	NA	NA	NA	NA	NA	NA	NA	NA
	3.3	NA	NA	NA	NA	NA	NA	NA	NA
	3.4	NA	NA	NA	NA	NA	NA	NA	NA
	Assessor's judgement	Low	Low	Low	Low	Low	Low	Low	Low
4. Measurement of the outcome	4.1	PN	PN	PN	PN	PN	PN	PN	PN
	4.2	PN	PN	PN	PN	NI	PN	PN	NI
	4.3	N	N	N	N	NI	N	N	NI
	4.4	NA	NA	NA	NA	PY	NA	NA	PY
	4.5	NA	NA	NA	NA	PN	NA	NA	PN
	Assessor's Judgement	Low	Low	Low	Low	Some concerns	Low	Low	Some concerns
5. Selection of the reported result	5.1	PY	PY	PY	PY	PY	PY	PY	PY
	5.2	PN	PN	PN	PN	PN	PN	PN	PN
	5.3	PN	PN	PN	PN	PN	PN	PN	PN
	Assessor's Judgement	Low	Low	Low	Low	Low	Low	Low	Low
Overall	Assessor's Judgement	Some concerns	Low	Low	Some concerns	Some concerns	Low	Low	Some concerns
Note		NP	NP	NP	NP	NP	NP	NP	NP

Y, yes; PY, probably yes; N, no; PN, probably no; NI, no information; NA, not applicable; NP, not pre- register openly available study

…Continuation1 of Appendix Table 3b. Detailed assessment of RoB 2.0 tool.

Domain	Reference	Logothetis and Martinez-Welles, 1995	Mamajiwala et al, 2018	Mohan and Jagannathan, 2016	Rani et al, 2014	Reddy et al, 2012	Retamal- Valdes et al, 2017	Saini, 2015	Sawhney et al, 2015
1. Randomization process	**1.1**	PY	PY	PY	PY	PY	Y	Y	PY
	1.2	NI	NI	NI	NI	NI	Y	Y	NI
	1.3	PN	PN	PN	PN	PN	PN	PN	PN
	Assessor's Judgement	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Low	Low	Some concerns
2. Deviations from intended interventions	**2.1**	NI	NI	NI	NI	NI	Y	N	NI
	2.2	NI	NI	NI	NI	NI	N	N	NI
	2.3	PN	PN	PN	PN	PN	PN	NA	PN
	2.4	NA	NA	NA	NA	NA	NA	NA	NA
	2.5	NA	NA	NA	NA	NA	NA	NA	NA
	2.6	PY	PY	PY	PY	PY	PY	PY	PN
	2.7	NA	NA	NA	NA	NA	NA	NA	PN
	Assessor's Judgement	Low	Low	Low	Low	Low	Low	Low	Some concerns
3. Mising outcome data	**3.1**	Y	PY	Y	Y	PY	Y	Y	Y
	3.2	NA	NA	NA	NA	NA	NA	NA	NA
	3.3	NA	NA	NA	NA	NA	NA	NA	NA
	3.4	NA	NA	NA	NA	NA	NA	NA	NA
	Assessor's judgement	Low	Low	Low	Low	Low	Low	Low	Low
4. Measurement of the outcome	**4.1**	PN	PN	PN	PN	PN	PN	PN	PN
	4.2	PN	PN	PN	PN	PN	PN	PN	PN
	4.3	N	NI	NI	NI	NI	NI	N	NI
	4.4	NA	PY	PY	PY	PY	PY	NA	PY
	4.5	NA	PN	PN	PN	PN	PN	NA	PN
	Assessor's Judgement	Low	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Low	Some concerns
5. Selection of the reported result	**5.1**	PY	PY	PY	PY	PY	Y	Y	PY
	5.2	PN	PN	PN	PN	PN	N	N	PN
	5.3	PN	PN	PN	PN	PN	N	N	PN
	Assessor's Judgement	Low	Low	Low	Low	Low	Low	Low	Low
Overall	**Assessor's Judgement**	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Low	Some concerns

Note		NP	NP	NP	NP	NP	Registered Protocol	Registered Protocol	NP

Y, yes; PY, probably yes; N, no; PN, probably no; NI, no information; NA, not applicable; NP, not pre- register openly available study protocol

Continuation2 of Appendix Table 3b. Detailed assessment of RoB 2.0 tool.

Domain	Reference	Sethi et al, 2019	Shetty et al, 2013	Swaminathan et al, 2014	Waghamare et al, 2018	NCT02319668
1. Randomization process	**1.1**	Y	PY	PY	PY	PY
	1.2	Y	NI	NI	NI	NI
	1.3	PN	PN	PN	PN	PN
	Assessor's Judgement	Low	Some concerns	Some concerns	Some concerns	Some concerns
2. Deviations from intended interventions	**2.1**	NI	NI	NI	NI	Y
	2.2	PN	NI	NI	NI	PN
	2.3	NA	PN	PN	PN	PN
	2.4	NA	NA	NA	NA	NA
	2.5	NA	NA	NA	NA	NA
	2.6	PY	PY	PY	PY	PY
	2.7	NA	NA	NA	NA	NA
	Assessor's Judgement	Low	Low	Low	Low	Low
3. Mising outcome data	**3.1**	Y	PY	Y	PY	Y
	3.2	NA	NA	NA	NA	NA
	3.3	NA	NA	NA	NA	NA
	3.4	NA	NA	NA	NA	NA
	Assessor's judgement	Low	Low	Low	Low	Low
4. Measurement of the outcome	**4.1**	PN	PN	PN	PN	PN
	4.2	PN	PN	PN	PN	PN
	4.3	PN	NI	NI	N	NI
	4.4	NA	PY	PY	NA	PY
	4.5	NA	PN	PN	NA	NI
	Assessor's Judgement	Low	Low	Some concerns	Low	High
5. Selection of the reported result	**5.1**	PY	PY	PY	PY	Y
	5.2	PN	PN	PN	PN	PN
	5.3	PN	PN	PN	PN	PN
	Assessor's Judgement	Low	Low	Low	Low	Low
Overall	**Assessor's Judgement**	Low	Some concerns	Some concerns	Some concerns	High
Note		NP	NP	NP	NP	Registered Protocol

Y, yes; PY, probably yes; N, no; PN, probably no; NI, no information; NA, not applicable; NP, not pre- register openly available study protocol

Appendix Table 4. The ranking probability of each treatment to be considered the 1st choice of interest, the second, the third, the fourth, as well as the overall % SUCRA values for treatment effectiveness.

Ranking	**Interventions (ranking probabilities in %)**									
	CHX 0.12%	**CHX 0.2%**	**ClO_2**	**CPC**	**HRB**	**HVE**	**OZ**	**PI**	**Control**	**Temp. CHX 0.2%**
Best (1st)	16.9	3.5	1.6	8.0	7.0	1.3	19.2	11.3	0.0	31.2
2nd	11.2	11.3	8.0	11.8	8.7	2.2	12.9	10.6	0.0	23.3
3rd	8.2	23.0	13.7	12.8	6.8	3.9	9.6	7.3	0.0	14.7
4th	6.2	25.9	23.0	11.6	7.9	4.2	6.4	5.3	0.0	9.5
SUCRA values (%)	53.0	66.4	59.0	55.9	44.4	31.5	57.8	44.2	9.1	78.6

CHX, chlorhexidine; ClO_2, chlorine dioxide, CPC, cetylpiridinium chloride; HRB, herbal substance related treatment; HVE, high volume evacuator; OZ, ozone; PI, povidone iodine; Control, any non- active intervention (water, normal saline, no treatment); SUCRA, surface under the cumulative ranking value; temp CHX, tempered (47^0C) chlorhexidine

Appendix Table 5. Quantitative data from individual single studies for pathogen load (colony counts*) after aerosol inductive dental procedure. The minus sign (-) shows better effect for 1st reported group in reducing pathogen load and vice versa. Bold indicate statistically significant comparisons.

#	Study ID	Dental procedure/ Setting	Comparison	MD (95% CIs)*	P-value
1	Dawson et al, 2016	Enamel clean- up after orthodontic fixed appliance debonding with slow- speed handpiece and tungsten carbide bur (*simulated pharynx level*)	CHX 0.2% as PMR vs. Sterile water PMR CHX 0.2% as PMR vs. No rinse	0.0 (-2.3, 2.3) 2.5 (0.5, 4.5)	1.0 **0.01**
		Enamel clean- up after orthodontic fixed appliance debonding with slow- speed handpiece and tungsten carbide bur (*simulated respiratory alveoli level*)	CHX 0.2% as PMR vs. Sterile water PMR CHX 0.2% as PMR vs. No rinse	0.4 (-1.1, 1.9) 1.2 (-1.1, 3.5)	0.60 0.31
2	Jawade et al, 2016	Use of coolants during ultrasonic scaling	CHX 0.12% vs. PI coolant CHX 0.12% vs. Water coolant PI vs. Water coolant	-33.3 (-55.3, -11.2) -97.3 (-117.5, -77.1) -64.1 (-91.9, -36.2)	**0.003** **<0.001** **<0.001**
3	Logothetis and Martinez- Welles JM, 1995	Air- polishing	CHX 0.12% as PMR vs. HRB as PMR Water as PMR vs. HRB as PMR HRB as PMR vs. Water as PMR	-71.2 (-79.7, -62.7) -69.5 (-80.2, -58.8) 1.7 (-11.2, 14.6)	**<0.001** **<0.001** 0.80
4	Mamajiwala et al, 2018	Use of solution extracts in DUWLs during ultrasonic scaling (aerobic counts)	CHX vs. CIN in DUWLs CHX vs. Water in DUWLs CIN vs. Water in DUWLs	32.5 (-15.7, 80.7) -814.0 (-872.1, -755.9) -846.5 (-906.1, -786.9)	0.19 **<0.001** **<0.001**
		Use of solution extracts in DUWLs during ultrasonic scaling (anaerobic counts)	CHX vs. CIN in DUWLs CHX vs. Water in DUWLs CIN vs. Water in DUWLs	-57.1 (-69.1, -45.1) -318.2 (-338.0, -298.4) -261.1 (-282.2, -240.0)	**<0.001** **<0.001** **<0.001**
5	Purohit et al, 2009	Comparison between 2 dental procedures in the presence of CHX 0.12% PMR	Ultrasonic scaling vs. tooth restoration through high- speed handpiece	1.6 (-0.5, 3.7)	0.13
		Comparison between 2 dental procedures without PMR	Ultrasonic scaling vs. tooth restoration through high- speed handpiece	-13.1 (-16.3, -9.9)	**<0.001**

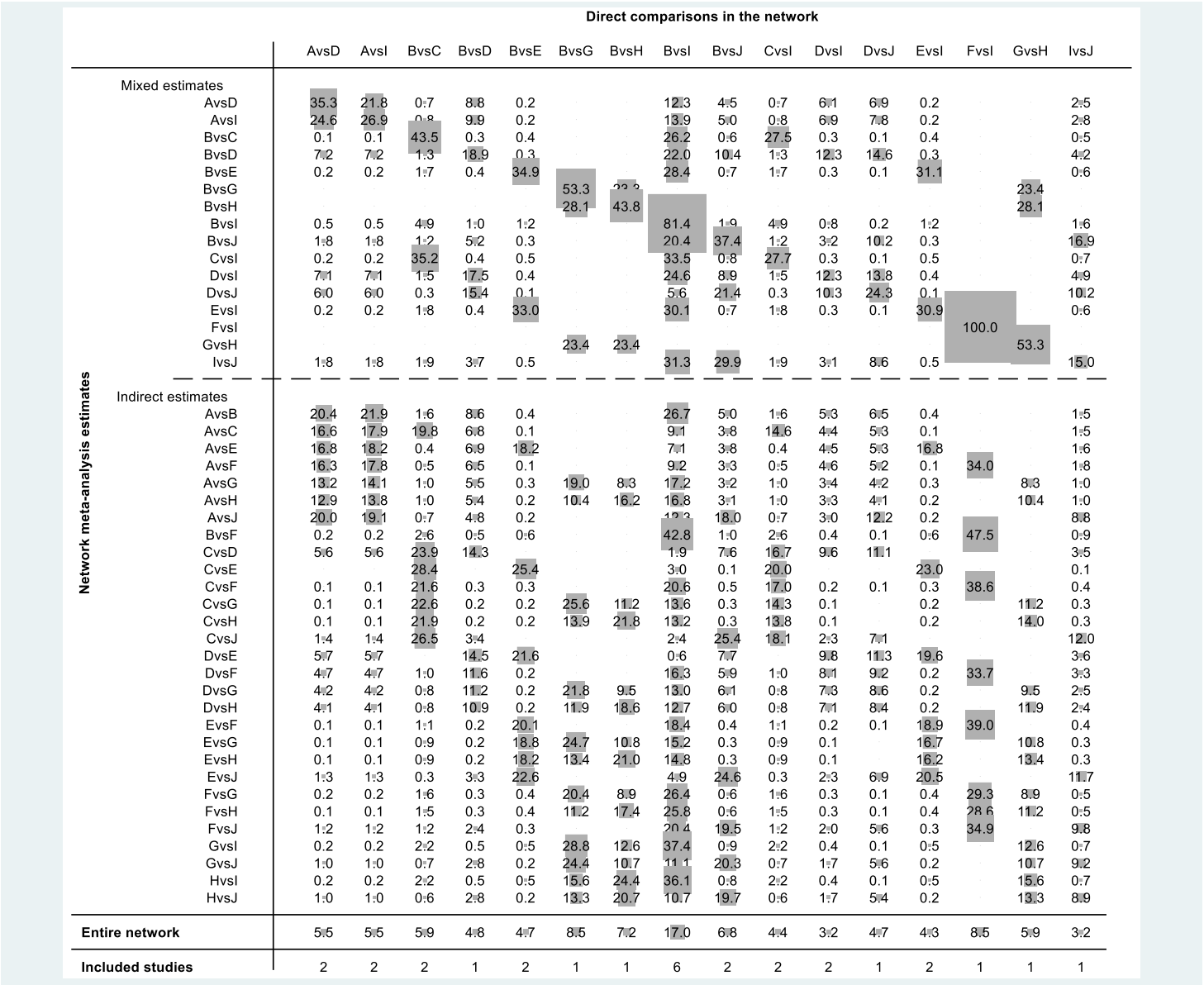
6	Sethi et al, 2019	Use of coolants during ultrasonic scaling	CHX 0.2% vs. CIN coolant CHX 0.2% vs. Water coolant CIN vs. Water coolant	51.5 (31.5, 71.5) -768.8 (-864.2, -673.4) -820.3 (-915.4, -725.2)	**<0.001** **<0.001** **<0.001**
7	Toroglou et al, 2001	Comparison between 2 orthodontic procedures	Debonding/ composite removal (air turbine handpiece, with water cooling and slow speed evacuation) vs. routine orthodontic practices without handpiece, but with slow speed evacuation	49.2 (19.4, 79.0)	**0.001**

* in CFUs (colony forming units) as reported in individual studies (no log-transformation of data); CHX, pre-procedural mouthrinse; CIN, cinnamon; DUWL, dental unit waterlines; HRB, herbal; PI, povidone iodine; PMR, pre- procedural mouth rinse

Appendix Table 6. Sensitivity network meta-analysis (NMA) mean differences in logCFUs (colony forming units), after omitting the studies of Gupta, 2014 and Saini, 2015. Comparisons are indicated by the column vs the row defining the intervention prior to ultrasonic scaling. Negative (-) mean differences are in favor of the column presented interventions, indicating reduced pathogen load. Mean differences for comparisons in the opposite direction may be obtained through conversion of negative to positive values and vice versa.

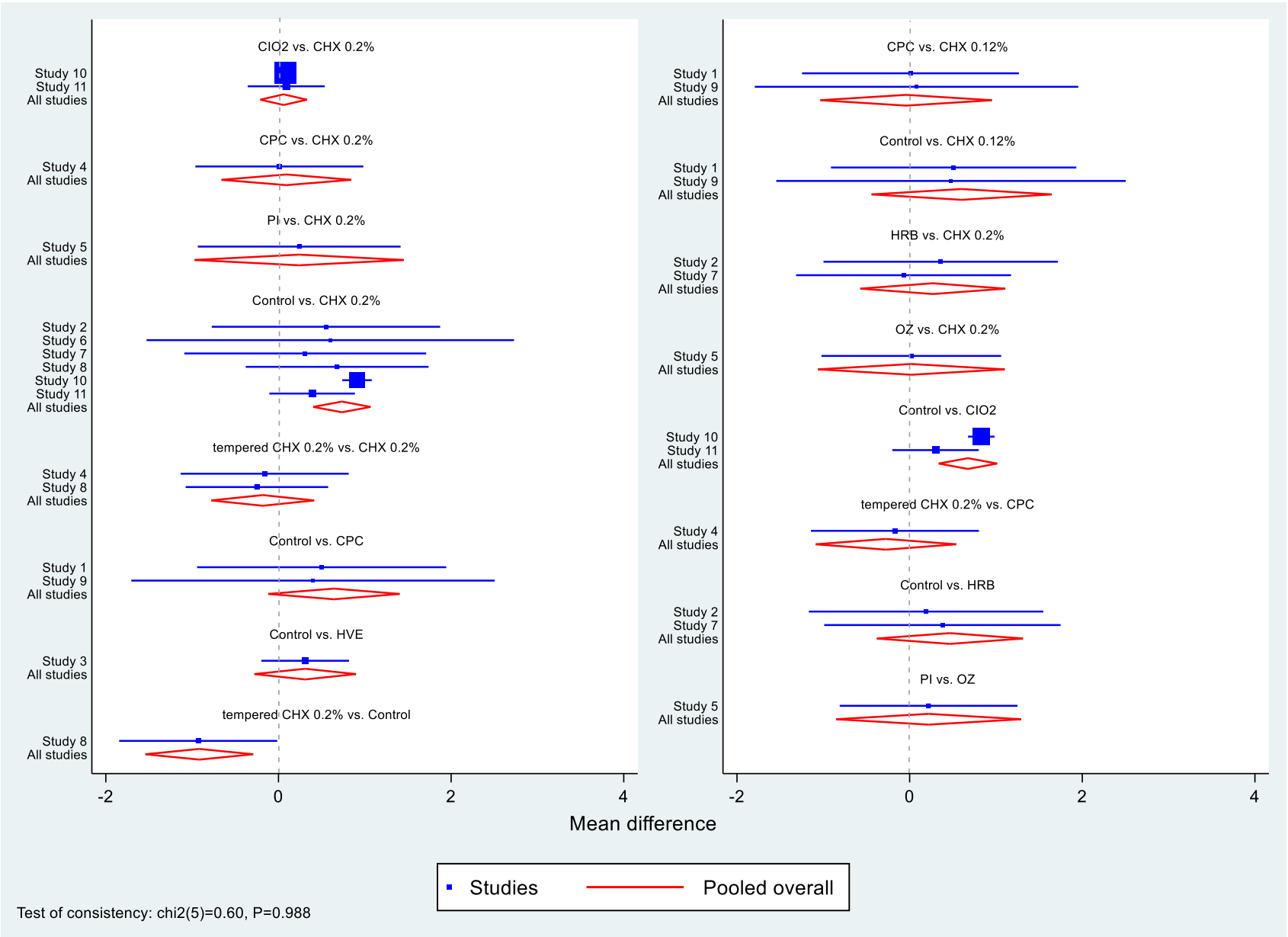
CHX 0.12%									
0.22 (-0.89,1.33)	temp. CHX 0.2%								
-0.51 (-1.53,0.51)	-0.73 (-1.34,-0.12)	Control							
-0.31 (-1.88,1.27)	-0.53 (-1.83,0.78)	0.20 (-1.04,1.45)	PI						
-0.09 (-1.57,1.39)	-0.31 (-1.49,0.88)	0.42 (-0.69,1.54)	0.22 (-0.81,1.25)	OZ					
-0.20 (-1.34,0.94)	-0.42 (-1.21,0.37)	0.31 (-0.20,0.82)	0.11 (-1.24,1.45)	-0.11 (-1.34,1.11)	HVE				
-0.05 (-1.55,1.45)	-0.27 (-1.50,0.96)	0.46 (-0.67,1.58)	0.25 (-1.36,1.87)	0.03 (-1.49,1.56)	0.15 (-1.08,1.38)	HRB			
-0.02 (-1.00,0.95)	-0.24 (-1.02,0.54)	0.49 (-0.26,1.23)	0.28 (-1.10,1.67)	0.06 (-1.21,1.34)	0.18 (-0.72,1.08)	0.03 (-1.28,1.34)	CPC		
-0.18 (-1.28,0.92)	-0.40 (-1.08,0.29)	0.33 (-0.14,0.80)	0.13 (-1.12,1.38)	-0.09 (-1.22,1.03)	0.02 (-0.67,0.71)	-0.13 (-1.30,1.04)	-0.15 (-0.97,0.66)	ClO2	
-0.07 (-1.12,0.98)	-0.29 (-0.85,0.28)	0.44 (0.04,0.85)	0.24 (-0.93,1.41)	0.02 (-1.02,1.06)	0.13 (-0.51,0.78)	-0.01 (-1.13,1.10)	-0.04 (-0.78,0.69)	0.11 (-0.32,0.54)	CHX 0.2%

Appendix Figure 1. Contribution plot for the aerosol bacterial load network under ultrasonic scaling. Size of squares is proportional to the weight attributed to the direct summary estimate for the estimation of the network pooled effects.

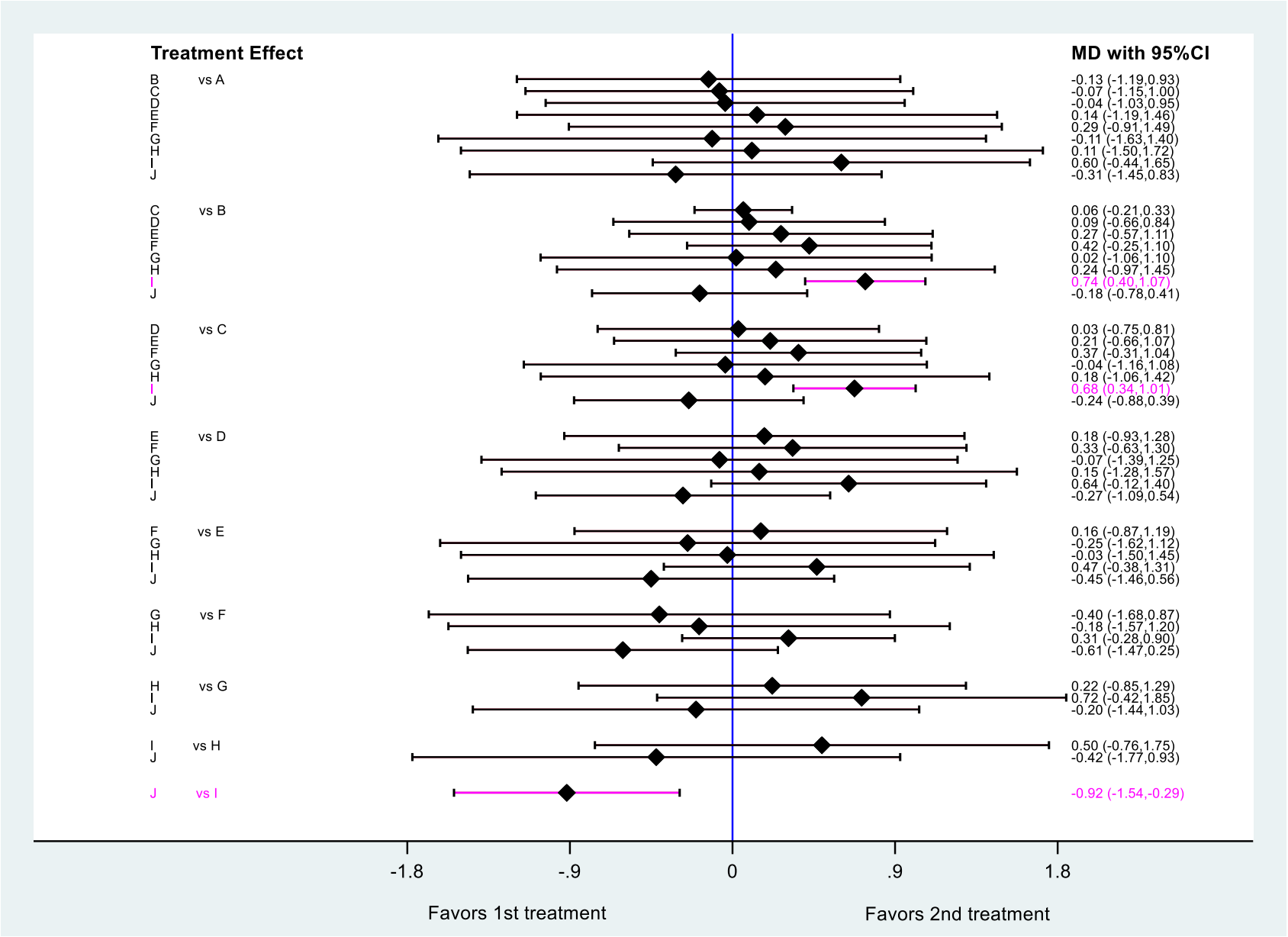


A, CHX 0.12%; B, CHX 0.2%; C, ClO_2; D, CPC; E, HRB; F, HVE; G, OZ; H, PI; I, Control; J, tempered CHX 0.2%

Appendix Figure 2. Forest plot of observed pairwise comparisons in the (network meta-analysis) NMA across competing interventions with regard to mean differences in post- procedural bacterial colony forming units (log_{10}CFUs).

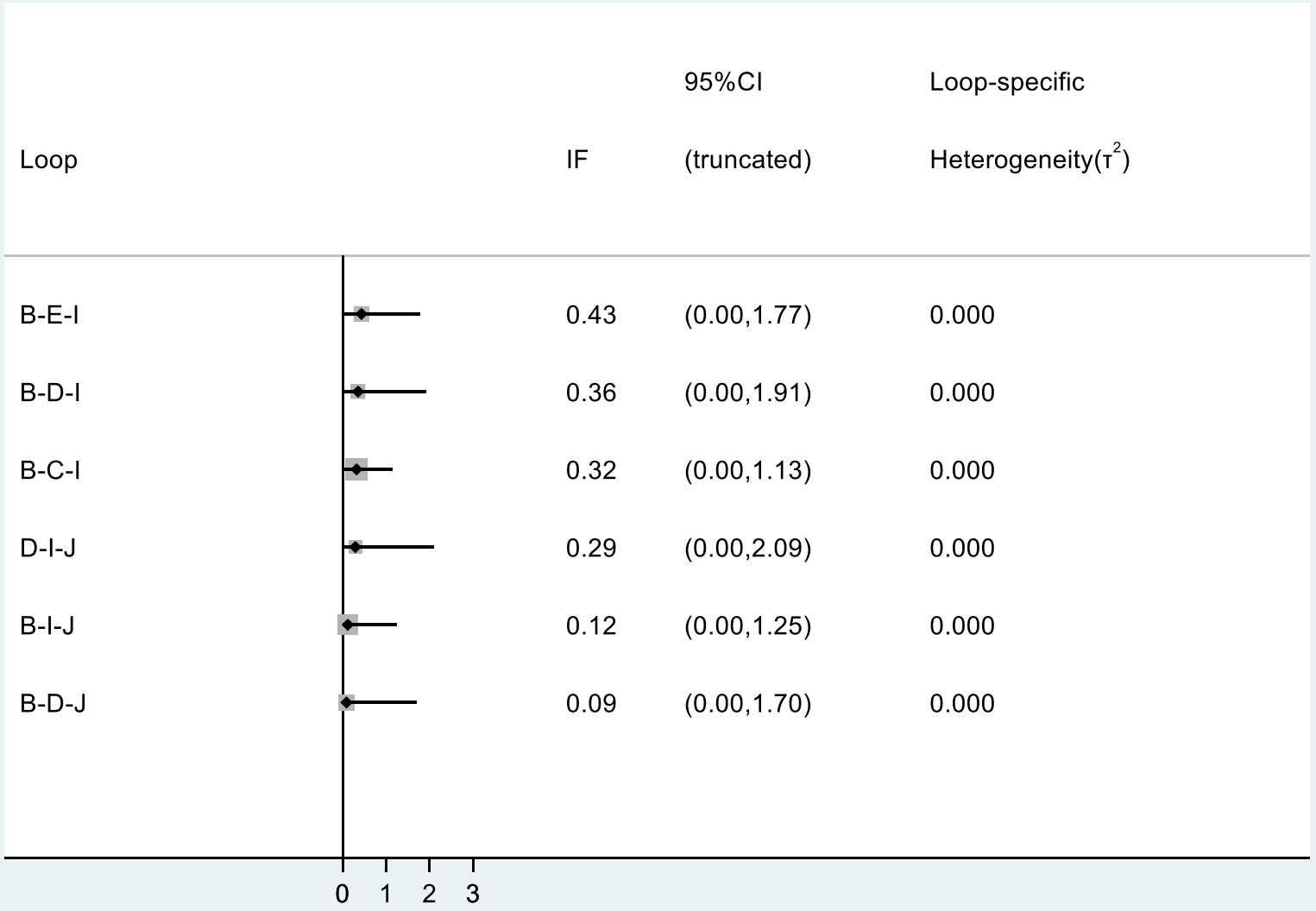


Appendix Figure 3. Interval plot, allowing for graphical representation of effect sizes (and respective 95% CIs), by treatment comparisons across the network

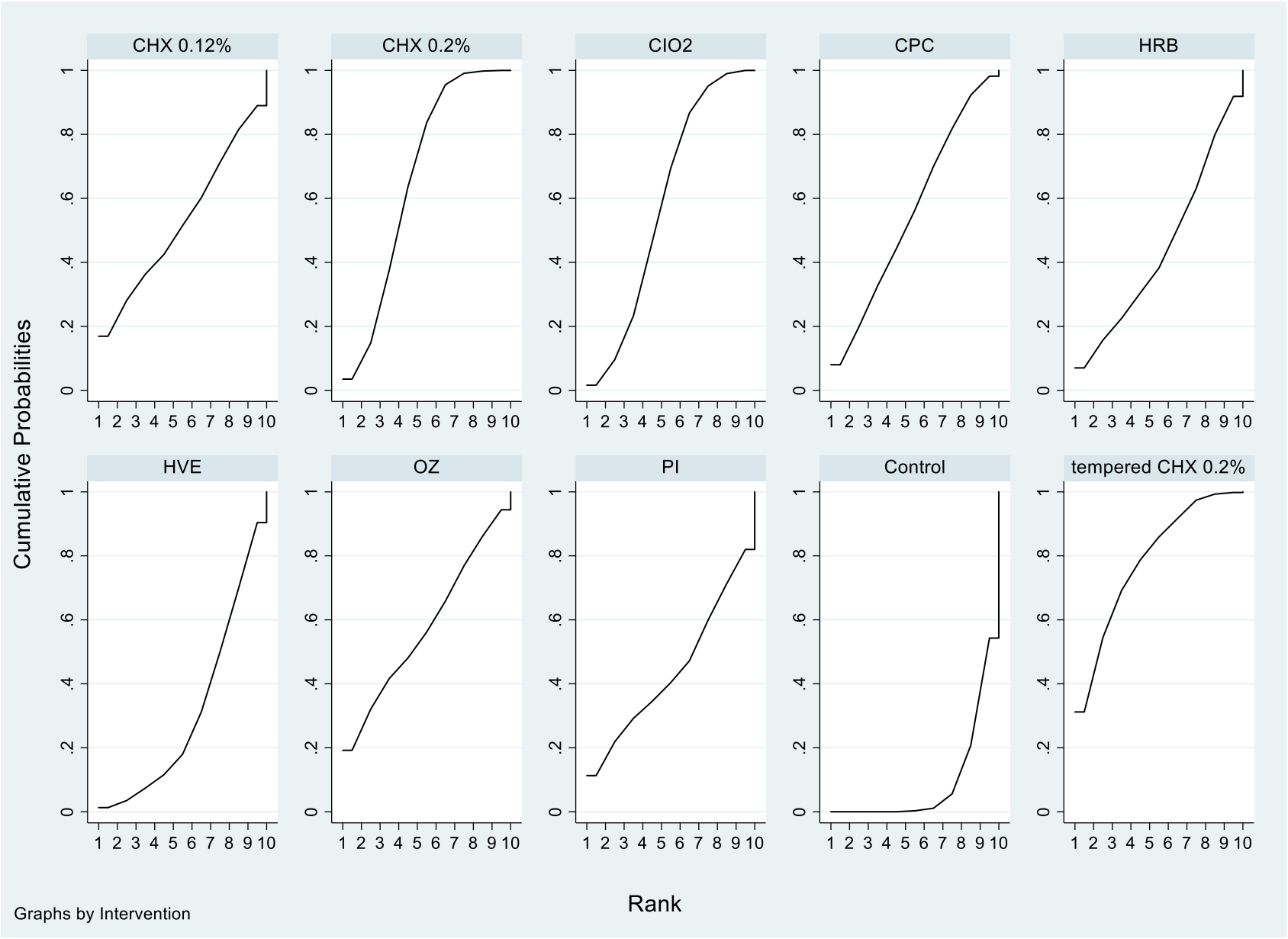


A, CHX 0.12%; B, CHX 0.2%; C, ClO_2; D, CPC; E, HRB; F, HVE; G, OZ; H, PI; I, Control; J, tempered CHX 0.2%

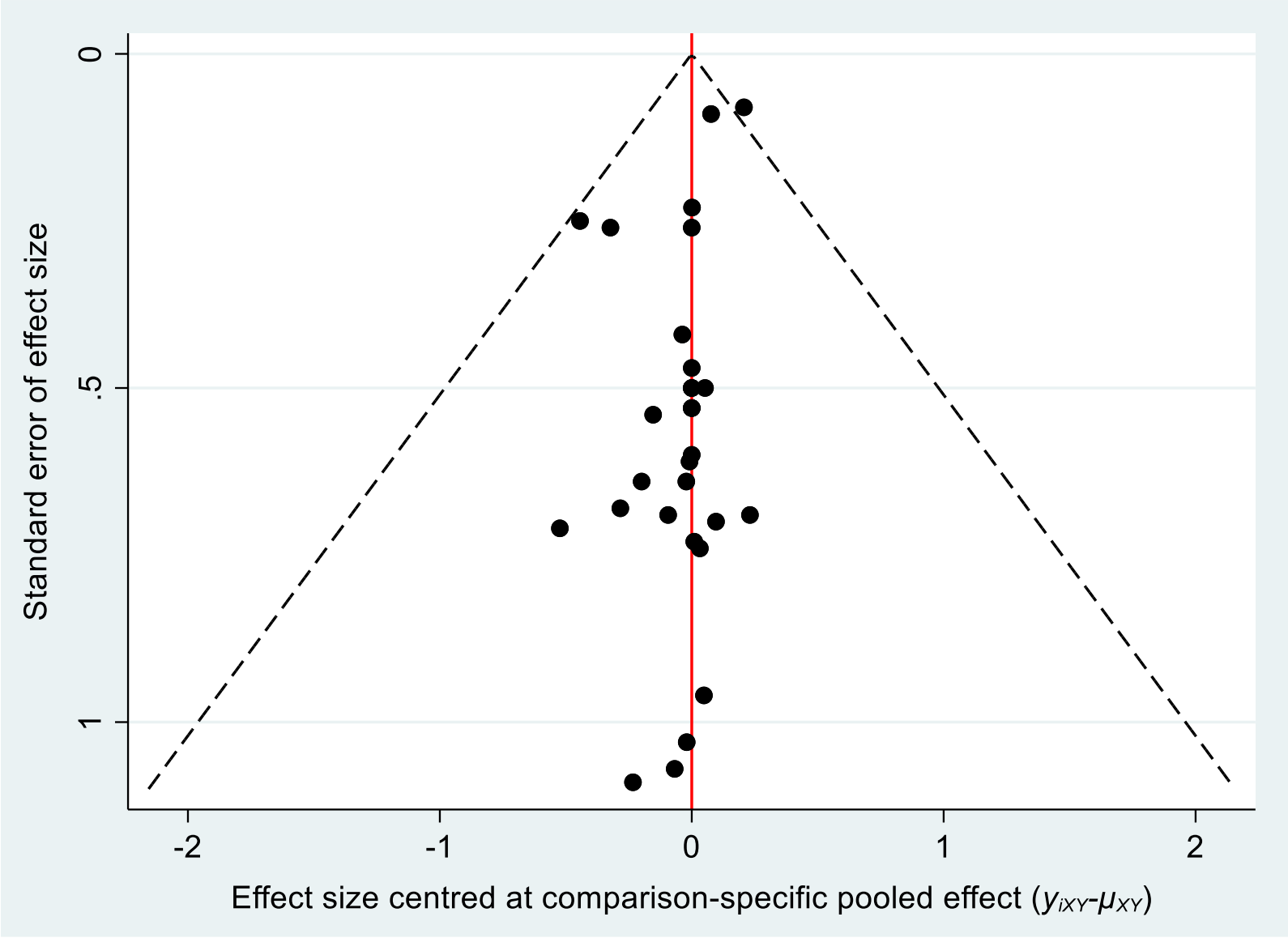
Appendix Figure 4. Inconsistency plot for the differences between direct and indirect estimates for each closed loop of evidence.



Appendix Figure 5. Cumulative rank probabilities for the overall effectiveness of each competing treatment. Surface under the curve corresponds to the SUCRA values.



Appendix Figure 6. Comparison adjusted funnel plot for the aerosol bacterial load network for publication bias. The red line represents the null hypothesis that the study-specific effect sizes are not different from the comparison-specific pooled effect estimates, respectively.



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